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BENIGN AND MALIGNANT TUMORS OF THE VULVA

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The skin and accessory cutaneous structures of the vulva occupy an important relationship to the vulval integument of the human female. The generally benign character of simple tumors developing in these structures has created little respect for their occasional malignant propensities. The design of metaplasia and malignant change in these innocent tumors is rarely emphasized. All too often they are described merely as small vulvar lesions when as a matter of fact they are often the key to a better understanding of the development and behavior of malignant growths in this area. My associates and I believe that a better general understanding of benign tumors of the vulva is an important aspect of preventive gynecology and is essential for the proper insight and control of vulvar cancer.

BENIGN TUMORS OF THE VULVA

Of Connective Tissue Origin.—In the group of benign tumors of connective tissue origin are the fibromas, leiomyofibromas, leiomyomas and lipomas. The rarer hemangiomas, lymphangiomas, neuromas and enchondromas are mentioned merely to complete the list.

The fibromas and leiomyofibromas of the vulva are not common. There were but nine recorded cases in thirty-nine years in the files of the University Hospital. The fibromas, leiomyofibromas and leiomyomas vary in size from 0.5 cm. to huge pedunculated masses. They are discrete and moderately firm to palpation and the overlying skin tends to be thick. The leiomyomas are notably soft to palpation and may show ulceration and infection in certain areas. They may arise as tumors of the round ligament or they may initiate primarily in the vulva. Fibromas and fibroleiomyomas originating in the vulva reveal a predominance of fibrous tissue, while those arising from the round ligaments and the long pedicled vulval tumors usually have an increased amount of smooth muscle tissue. Taussig [1] quotes Leonard as finding 22.5 per cent of these tumors undergoing sarcomatous changes. At the University Hospital we found these changes in one of the nine cases—an incidence of 11 per cent.

The symptoms caused by fibromas and fibroleiomyomas of the vulva are due chiefly to the weight and location of the mass. They may cause distress on locomotion, and mild urethral irritation may occur if the mass pulls or involves the urethra. Likewise the weight may cause urinary incontinence or increased frequency by interfering with the sphincter mechanism. The treatment is surgical extirpation. The tissue removed should always be examined by a competent pathologist.

Lipomas of the vulva are less common than fibromas. There were no recorded cases at the University Hospital. Lipomas of the vulva are prone to be located more laterally on the labia majora or in the genitocrural folds. They are seen also on the medial side of the upper part of the thigh or in the gluteal areas. Taussig [1] describes the smaller ones as "polyp-like," while the larger ones are "apron-like." Lipomas are lobulated and soft and have broader bases than fibromas. There is no danger of malignant change, and simple surgical removal is the treatment.

Hemangiomas of the vulva are reported as rare. Three cases have been recorded at the Gynecology Clinic of the University Hospital in the past ten years, an approximate ratio of 1 case to each 19,000 pelvic examinations. These tumors present varied appearances dependent entirely on their predominating type of tissue present. They may vary from red to brown and from maculopapular to small lobulated soft tumors. The more complex variety, such as the endotheliomas and cylindromas, appear as slow growing, semispherical tumors. The more complex the pathologic pattern, the greater the danger of invasion. Improper treatment may lead to the development of angiosarcomatous change. Our third case, a hemangioma-endothelioma cylindromatosum, presented a rounded semifirm mass the size of a small orange on the left labium majus. The treatment is surgical removal of the tumor, together with ample surrounding tissue.

The lymphangiomas, myxomas, neuromas, osteomas and enchondromas of the vulva are rare and complex tumors. Those interested in these rare tumors will find adequate descriptions in the various gynecologic-pathologic compendiums.

Of Epithelial Origin.—Benign tumors of the vulva of epithelial origin include true papillomas and those papillomas commonly termed condylomas, arising from residual pathologic irritation of subacute or chronic infections such as gonorrhea; hidradenomas or sweat-gland adenomas of the vulva; supernumerary vulval breast, which occasionally undergoes carcinomatous change; endometriosis, and the many varieties of cystic tumors of the vulva.

The condylomata acuminata are usually multiple papillated excrescences. They may vary from the size of a wheat seed to that of a large orange. They may be filiform, multiple, widespread or grouped cauliflower-like about the labia majora or perineum or in the genitocrural folds. The larger ones become ulcerated, may

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1. Taussig, F. J.: Obstetrics and Gynecology, edited by A. H. Curtis, Philadelphia, W. B. Saunders Company 1: 586 (chap. 88) 1933.

bleed easily and, when secondarily infected, become exceedingly painful. Their history is one of much more rapid evolution than those of the senile type. In pregnancy they have a tendency to increase and multiply in size and number.

Small tumors of this kind can be treated with caustic keratolytic drugs such as silver nitrate, trichloroacetic

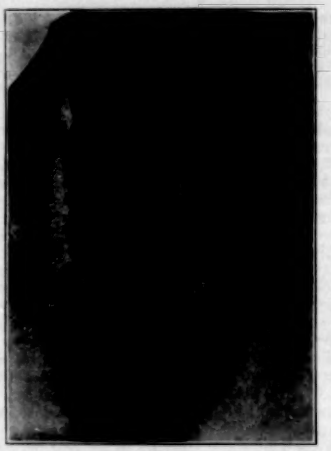

Fig. 1 (Mrs. M. O.).—Inoperable primary melanoblastoma of clitoris. Death occurred two weeks after this photograph from ruptured subcapsular hepatic metastases producing an extensive hemoperitoneum. Autopsy revealed extensive metastases.

acid or salicylic acid ointments, but the surrounding tissue should be protected with petrolatum. It may be necessary first to clean up an associated tineal infection or to use various drying agents to clear the contiguous dermatitis. The actual cautery is used by many dermatologists to care for the smaller lesions. If untreated and long neglected, condylomas may undergo malignant change. Such was the case with two Negro patients, one with neoplastic change in a papilloma of the genitocrural fold and the other with the same in a perineal papilloma.

True papillomas are usually found in older patients and more commonly in persons past the menopause. The senile papillomas of the vulva are usually well circumscribed and are raised wartlike slightly above the surface (fig. 2). They may be multiple or lobulated. Some are single pedicled, multilobulated tumors. The surrounding vulval skin often presents evidence of senile atrophy. Patients often report that these wartlike bodies have been present for years.

Among our patients, carcinoma was found to have originated in a senile papilloma in five instances, an incidence, based on the number of papillomas recorded in diagnoses, of 23 per cent. This incidence is undoubtedly high and probably does not truly represent the relationship, since many of the smaller papillomas were probably not recorded. Nevertheless, here exists a very real opportunity for prevention. This relationship should be recognized and all vulval papillomas should be treated as potential carcinomas. Surgical excision with ample removal of tissue near the base is the best therapy. Because these papillomas may undergo malignant change, tissue removed should always be submitted for study by a competent pathologist.

Hidradenomas or sweat-gland adenomas of the vulva are unusual. We have been able to collect fifteen cases from the files at the University of Michigan. A detailed histopathologic report of these tumors will appear in a later publication.

The sweat-gland adenomas of the vulva are usually small, from pea to walnut size, single, generally unilateral and usually located in the labia majora or minora. The tumor is usually cystic but may be solid. These adenomas have been described as intracystic papillomas.[2]

The hidradenomas of the vulva are discrete and have definite, well circumscribed boundaries. They are freely movable over the underlying deeper tissues. The skin covering the small tumors is usually intact, although ulceration of the skin can occur. Its color does not differ from the surrounding tissue. Unless ulcerated and secondarily infected, or located on the mesial side of the introitus in such a manner as to cause dyspareunia, these adenomas produce no symptoms. The tumors usually are very slow growing, requiring from one to many years for their evolution. The majority are benign, although 27 per cent are distinctly locally invasive in character or possess potential ability to become malignant. The only treatment necessary is simple excision, which in most cases can be effected easily under local anesthesia. Because of their local invasive characteristics it is well to include ample tissue in the area of excision.

The vulval supernumerary breasts or persistent milk ridge breast tissue tumescences are most unusual. They are usually soft, spherical, semicystic masses, located in the interlabial fossae or medial side of the labium majus. During pregnancy they enlarge and behave similarly to other supernumerary breasts. Mengert [3] reported an interesting example of bilateral tumors. Greene [4] described such a tumor with adenocarcinomatous and epidermal carcinomatous changes. The treatment is surgical removal with subsequent pathologic examination of the tissue.

Endometrioma of the vulva is rare. In 1929 at the University Hospital a small endometrioma was removed from the mons pubis of a young woman. The tumor

Fig. 2.—Carcinoma of the vulva, clinical stage 1, Taussig. Tumor from 1 to 3 cm. in average diameter. No palpable metastases. This case showed early carcinoma in a papilloma.

had been present for about two years and the history cited periodic swelling. A microscopic examination by our pathologist showed typical endometrium. Any such endometriomas can be removed surgically under local anesthesia.

2. Hoeck, Werner: Zentralbl. f. Gynäk. 50:2757-2760 (Oct. 23) 1926. Rolleston, H. D.: Brit. J. Dermat. 14:83-86, 1902.
3. Mengert, W. F.: Am. J. Obst. & Gynec. 29:891-892 (June) 1935.
4. Greene, H. F.: Am. J. Obst. & Gynec. 31:660-663 (April) 1936.

The benign cystic tumors of the vulva are rather commonly found. Many systems or etiologic classifications are recorded in the literature. For practical clinical purposes we favor Taussig's suggestion based on cyst content: sebaceous cysts, serous cysts and mucous cysts.

Sebaceous cysts, also termed atheromas, may vary from the size of a pinhead to that of a hen's egg. When

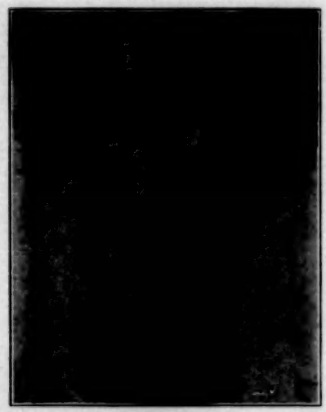

Fig. 3.—Carcinoma of the vulva, clinical grade 2, Taussig. Tumor from 4 to 7 cm. in diameter. No palpable metastases.

the gland duct becomes occluded, the cystic cavity fills with inspissated cheesy sebaceous material. These cysts tend to be multiple and favor the mesial border of the labia majora or either side of the labia minora. Their color varies from yellowish to gray yellow. It is not uncommon for them to become secondarily infected. Dealy,[5] although not specifically mentioning vulval sebaceous cysts, states that from 2 to 3 per cent become malignant. The symptoms, if any, are dependent on the size of the cyst and on whether or not it is infected. The surgical removal of these cysts or treatment by electrocautery is a simple office procedure.

The more common thin walled serous cysts are often found on the two upper quadrants of the vulva, especially in the labia minora. They vary from pea to plum size and tend to be single. Their etiology is of more interest to a gynecologic pathologist than to one who is clinically minded. Fourteen of this type were seen at the University Hospital in 1938, an incidence of one to each 357 pelvic examinations. Treatment of these cysts is removal.

Bartholin cysts, most common of the mucous variety, lead in frequency. One hundred and nine cases were seen at the Gynecology Clinic in 1938, an incidence of one to each forty-six pelvic examinations. It is of interest to note that only twenty-three cases (21 per cent) presented symptoms, and of these only fourteen (13 per cent) required treatment. The fact that only nineteen cases (17.5 per cent) of the entire group showed clinical evidence of gonorrhea of the lower genital tract or residual inflammatory disease of the pelvis suggests the possibility of other than gonorrheal origin. Treatment of symptom-producing Bartholin cysts may be simple excision, enucleation of the cyst or aspiration of the cystic contents and obliteration of the cystic walls with escharotic chemicals.

5. Dealy, F. N.: Am. J. Surg. 36: 132 (April) 1937.

MALIGNANT TUMORS OF THE VULVA

Sarcoma of the vulva is rare. It may develop in the vulvar end of the round ligament or may be primary in the vulva. Sarcomatous change may occur in angiomatous vulval tumors.[6] Two cases of sarcoma of the vulva have been seen at the Gynecology Clinic of the University Hospital. Physicians in the state of Michigan have sent tissue from three other patients. One of our cases of sarcoma of the vulva has previously been reported by Morgan.[7]

The evolution of sarcoma of the vulva usually is rapid. The lesion is generally irregular, nodulated and covered with a thin layer of epidermis. It may resemble a fibroma of the vulva until ulceration and infiltration take place. Frank, quoted by Taussig,[6] states that the lymphatic glands are rarely affected, thus differing from carcinoma and melanoma of the vulva, but our cases all showed involvement of the inguinal glands. The incidence is low, occurring in about one case in every 10,000 pelvic examinations at the University Hospital. Those originating in the vulva are not uncommonly designated fibrosarcomas.

Some pathologists describe fibrosarcomas of the vulva as tending to remain localized, but actually these tumors may undergo wide hematogenous spread, as evidenced by two of our more recent cases. Once beyond local control, these tumors metastasize rapidly to most parenchymatous organs of the body. One of our cases evidenced metastases to the scalp and frontal bone. Clinical experience clearly indicates that radical vulvar surgery is the most successful treatment.

Metastatic malignant tumors of the vulva are rare. The records of the University Hospital reveal three cases of adenocarcinoma of the vulva associated with adenocarcinoma of the fundus; two cases of vulvar metastasis from chorio-epithelioma and one case of melanoma of the cheek presented a vulval metastasis. Interestingly enough, in the past five years we have performed biopsies on vestibular nodules from two patients. Because of the neoplastic cell type, the pathologist advised a check on the lungs for the primary lesion, and a bronchogenic carcinoma was found in each instance.

Fig. 4.—Carcinoma of the vulva, clinical grade 3, Taussig. Ulcer over 7 cm. in diameter or deeper infiltration or palpable gland metastases.

A careful review of our records for the past thirty-nine years reveals but three cases of primary melanoma of the vulva, an approximate incidence of one case to each 125,000 pelvic examinations. These tumors are usually lobulated, bluish black pigmented new growths. They grow rapidly and metastasize very early to distant organs. There is early invasion to the lymph nodes.

6. Taussig, F. J.: Amer. J. Obst. & Gynec. 33: 1017-1026 (June) 1937.
7. Morgan, H. S.: Am. J. Obst. & Gynec. 15: 861 (June) 1928.

Their relation to the pigmented blue-black moles is well known in other cutaneous areas and but little emphasized in the vulvar region. We have had the experience, on two occasions, of removing a small pigmented papillated mole, from the mons pubis in one case and the genitocrural fold in another case, only to have the pathologist report back "questionable early melanoblastoma, excision adequate but advise close observation." Emphasis on the proper care for these small pigmented moles would be excellent preventive medicine.

Two of the three melanomas of the vulva in our series were found to have their origin in the clitoris (fig. 1). While the treatment of this condition is surgical, it is important to remember that the primary growth may appear small and readily operable long after widespread metastasis has occurred. Consequently, x-ray examination of the chest, a very careful clinical history and a physical examination to rule out distant metastases should always be a part of the preoperative program. The prognosis is extremely poor, 100 per cent fatal in our series of three cases.

Basal cell carcinomas of the vulva are relatively rare. They appear as small indurated and ulcerated tumescences usually found on the labia majora. Six cases have been seen at the University Hospital. Three patients had rodent ulcers elsewhere on the skin of the body and in two cases there was more than one rodent ulcer on the vulva. Treatment is surgical extirpation. In the two cases followed for four and six years respectively there has been no recurrence of the vulval lesions.

Carcinoma of the vulva is the most common malignant neoplasm of the external female genitalia. In thirty-nine years at the University Hospital 201 separate cases were encountered; 128 cases proved by both biopsy and clinical examination were seen in the gynecology department; seventy-six additional positive biopsy or tissue specimens sent by physicians in the state of Michigan were examined in the pathology department, and the other seven cases were seen and diagnosed clinically in the gynecology department. It is impossible to compare accurately the incidence of carcinoma of the vulva with other malignant conditions of the female generative tract; however, it closely approximates 4 per cent. In the definite control period from July 1, 1931, to Jan. 1, 1938, of 1,026 cases of carcinoma of the female generative system there were forty-four cases of carcinoma of the vulva, or a ratio of 1 to 24.

Fig. 5.—Carcinoma of the vulva, clinical group 4, Taussig. Large ulcer with vaginal involvement or large cancerous lymph glands.

The vulval cancer is primarily a tumor of senility. The greatest age incidence is in the sixth to the seventh decade. The average age in our group was 60.92 years, while the median age was 61.73 years. It is of interest to note, in the light of Hall and Bagby's paper on "Carcinoma in the First Three Decades of Life,"[8] that three of our 128 patients were 30 years or less in age. There were seven Negro women, one was a Tawa Indian woman and the remainder were members of the white race. Four of the seven Negro patients also had latent syphilis (fig. 5).

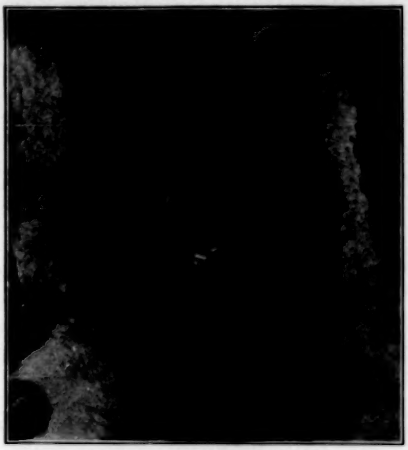

Fig. 6.—Carcinoma of the vulva, clinical group 5, Taussig. Far advanced with broken down glands and cachexia.

Taussig's five clinical stages of carcinoma of the vulva based on the size of the primary tumor and degree of involvement of the inguinal glands is the most practical. The 128 cases seen in the University Hospital were regrouped according to Taussig's classification (table 1). The presence of movable metastases of the inguinal gland, however, does not imply inoperability. Taussig[9] operated on 70 per cent of his patients and in 63 per cent achieved five year arrests. Later figures[9] revealed an absolute curability of 26 per cent, representing thirty of Taussig's sixty-seven treated patients. Figures 2, 3, 4, 5 and 6 illustrate each of these clinical types.

The average patient with carcinoma of the vulva procrastinates an amazing length of time before consulting a physician. The average patient seen at the University Hospital lost approximately fifty-six weeks, or thirteen months, before seeking treatment. Seventy-five per cent of our series fell into the last three stages of Taussig's clinical groupings (table 1). It is disheartening to review the many histories of patients treating themselves with "patent medicines" or receiving advice regarding treatment without examination.

The three cardinal symptoms of carcinoma of the vulva were pruritus (58 per cent), tenderness, soreness or actual pain (48 per cent) and "spotting" or irritating leukorrheal discharge (28 per cent). If one waits for the three principal signs of carcinoma of the vulva—tumor mass, ulceration or actual edema of one or both lower extremities—there is little hope for a

8. Hall, Norman, and Bagby, J. W.: Carcinoma in the First Three Decades of Life, J. A. M. A. 110: 703-706 (March 5) 1938.
9. Taussig, F. J.: Surg., Gynec. & Obst. 60: 477 (Feb. 15) 1935.

favorable prognosis. One fact stands out above all others in reviewing the symptoms of these patients—no patient with pruritus vulvae should be treated with medical nonchalance! To this warning might be added the admonition that the presence of any small tumor of the vulva, irrespective of the age of the patient, must be thoroughly examined and removed if carcinoma of the vulva is to be controlled.

At the University Hospital the treatment of carcinoma was based entirely on the principle of individualization. In a survey of treatment covering more than thirty-nine years, we have come to question seriously with McKelvey and McLennan [10] the advisability of continuing to use multiple methods of treatment.

Simple resection of the vulva with superficial resection of the inguinal glands and incomplete vulval surgery with coagulation technic have been abandoned. For precancerous conditions a simple vulvectomy may suffice but such cases, especially in the younger age group, should be kept under close surveillance.

Treatment of carcinoma of the vulva entirely by radiation therapy, whether by radium, x-rays or a combination of the two, has been most disappointing. Plate's [11] experience is similar to ours. He had no survivals after five years. We had but one survival after five years among the twenty-nine patients treated entirely by irradiation. Schreiner and Wehr [12] were of the opinion that radical coagulation and highly filtered x-rays or radium to the lymph-bearing areas was applicable to a larger number of cases. It has been our experience that the addition of irradiation to operation is of little benefit. The type and thoroughness of operation appears to be the most important factor!

Under the admirable leadership of Basset and Taussig, adequate treatment based on anatomicopathologic knowledge of malignant growths peculiar to this area is undergoing rapid development. In short, extensive vulvar surgery with superficial and deep bilateral inguinal resection, commonly known as the Basset technic, seems to give the most adequate assurance of favorable results. In the hands of Taussig,[1] nine of his eleven patients (81.8 per cent) were well after five years, while in 1935 thirty of his sixty-seven patients treated were well after five years.

TABLE 1.—*Carcinoma of the Vulva Regrouped According to Taussig's Clinical Groups*

	No. of Cases	Percentage
Group 1. Tumor 1-3 cm. average diameter, no palpable metastases	10	8
Group 2. Tumor 4-7 cm. diameter, no palpable metastases	22	17
Group 3. Ulcer over 7 cm. diameter or deeper infiltration, or palpable gland metastases	40	31
Group 4. Large ulcer with vaginal involvement or large cancerous lymph glands	43	34
Group 5. Far advanced with broken down glands and cachexia	13	10
Total	128	

The results from earlier methods of treatment in our clinic were far from encouraging. Only fourteen (10.9 per cent) of ninety-one patients with carcinoma of the vulva who were followed up lived five years or more after treatment, and of these only seven patients (5.45 per cent) are still living (table 2).

The observation that the number of five year arrests fall consistently into that group treated by surgery is convincing us that the better results are obtained by this method.

The control and prevention of carcinoma of the vulva rests squarely on two persons. The first is the patient herself, who should include an annual periodic pelvic examination with her once a year health check-up.

TABLE 2.—*Treatment of Carcinoma of the Vulva: 128 Cases*

	Number of Cases	Number Alive	Number Dead	Number Lost	No. of 5 Year Arrests	Per Cent
Surgery only	51*	15	23	13	8	7.4
Surgery and irradiation combined	27*	5	19	3	5	4.7
Irradiation only	29	2	21	5	1	0.9
Too advanced or refused	21	3	10	6	0	
Total	128	25	76	27	14	

* These two groups, seventy-eight patients, were treated by vulval surgery or by vulval surgery combined with irradiation. Because this group covers a period of thirty-nine years, including a large number of treatments consisting only of surgery, which would be considered inadequate at the present time, the number of five year arrests after treatment is obviously small.

This approach is the shortest and most successful prerequisite of any educational campaign against carcinoma. The second person to lend invaluable assistance to the prevention of carcinoma of the vulva is the local physician. Every family physician should be so imbued with preventive treatment that he will not fail those approaching him for complete periodic health examinations (pelvis always to be included). He should make it a point to examine every patient presenting herself with pruritus vulvae or other vulvar lesions.

SUMMARY

1. Metaplasia and malignant change in apparently innocuous vulvar tumors are inadequately emphasized. Papillomas, sebaceous cysts, pigmented moles, leiomyofibromas, vulvar breast tissue and sweat gland adenomas are some of the benign vulvar tumors which may, at a later date in a woman's life, degenerate to vulvar malignancy.

2. Treatment and care of the patient presenting herself with a vulvar cancer are tending to become more rational in the light of present anatomicopathologic knowledge of vulvar cancers. Vulval surgery combined with resection of superficial and deep inguinal lymph nodes, the so-called Basset technic, with modifications as outlined by Taussig, continues to be the best treatment for carcinoma of the vulva.

By stressing periodic pelvic examinations, cancer educational programs may materially assist in preventing cancer of the vulva. By paying attention to simple lesions and the benign tumors of the vulva, the physician may prevent carcinoma of the vulva.

1014 Rose Avenue.

10. McKelvey, John, and McLennan, C. E.: Staff Meet., Bull., Hosp. Univ. Minnesota **10**: 1-20 (No. 1) 1939.
11. Plate, W. P.: J. Obst. & Gynaec. Brit. Emp. **44**: 737-742 (Aug.) 1937.
12. Schreiner, B. F., and Wehr, W. H.: Surg., Gynec. & Obst. **58**: 1021-1026 (June) 1934.

Hammer Toe.—This is a condition in which the proximal phalanx of a toe is extended while the second and distal phalanges are flexed, causing a claw-like appearance. The second toe is most often involved. The condition may be congenital or acquired. Congenital hammer toe usually affects the second toe; acquired hammer toe is practically always secondary to some other deformity, such as pes valgoplanus, or talipes arcuatus.—Hauser, Emil D. W.: Diseases of the Foot, Philadelphia, W. B. Saunders Company, 1939.

THE SEX HORMONES

THEIR PHYSIOLOGIC SIGNIFICANCE AND USE IN PRACTICE

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No one except an active worker in the field of endocrinology can attempt to follow the enormous literature, physiologic, biochemical and clinical. Even the specialist must restrict himself to a single branch—in the present instance to the sex hormones. The general practitioner will be hopelessly bogged by the extent and scattering of the articles published which trench on advanced organic chemistry, minutiae of physiologic experimentation and interpretation of intricate assays. The conflicting, often uncritical, clinical reports eventually force him to rely on a hit or miss trial of therapy with "endocrine remedies" of which he ignores the source and often the dosage. In this paper I shall try to clarify the situation as well as this is possible in the present state of our knowledge and in particular to measure the therapeutic results reported, by the yardstick of my own experience.

When, years ago, Eppinger, Falta and Rudinger[1] proposed the concept of interaction of the various glands of internal secretion with its famous triangle, this was largely a hypothesis which was accepted with reserve. Today no one will question such interaction. It has become the fashion to call the adenohypophysis or prepituitary the master gland, but this concept is no longer tenable, first, because the hypophysis reacts so readily to the influence of the other glands of internal secretion as to rob it of this distinction and, second, because the adrenal appears fully as important as the prepituitary, and more vital for existence.

The hormones to be discussed belong to two distinct groups. The prepituitary hormones are of protein character and nothing in regard to their structure is known. The male and female sex hormones, as well as the adrenal androgen, belong to the steroid hormones, the molecular structures of which have been determined and their close relationship to cholesterol demonstrated.

Steroid Hormones (cyclopentenophenanthrene skeleton):
(*a*) Corticosterone with several companion hormones (adrenal cortical hormones $C_{20}O_{3-4}$) also one member of C_{19} group "adrenosterone"—male action.
(*b*) Progesterone $C_{21}O_2$.
(*c*) Male hormone C_{19}.
(*d*) Female hormone C_{18}.

Today it no longer suffices to regard the female as feminine and the male as masculine, since the two sexes have hormones of the opposite sex in their circulation and excretions. Every physician is familiar with the bisexual anlage in the human fetus in which for months the female (müllerian) and male (wolffian) ducts are equally well developed. This fetal, anatomic hermaphroditism, which is transitory, after puberty is replaced by a permanent chemical hermaphroditism. How great a role the sex hormones of the opposite sex (i. e., male hormone in the female and vice versa in the male) play in physiology or functional pathology is as yet an open question. It is possible that most often they occur as inactive intermediate metabolic products but that under certain conditions they may disturb the balance of sex sufficiently to produce symptoms. Moreover, these hormones are not strictly specific, some of the androgens and adrenal extracts, for example, showing estrogenic and progestational activity.[2]

To the prepituitary have been assigned some eight to ten hormonal functions.[3] Possibly when a more final analysis can be attempted greater simplification will be attained: a stimulating hormone, affecting growth and metabolism and another stimulator of the various glands of internal secretion, a portion of which is now called the gonadotropic hormone, not sex specific, which activates in the female the follicle and the corpus luteum; in the male, the germinal and interstitial cells.

PREPITUITARY HORMONES

Beyond the fact that prepituitary hormones are closely associated with a protein molecule, lipoid insoluble, thermolabile and sensitive to strong acids and alkalis, little is known despite the immense amount of work that has been concentrated on their identification. By various methods it has been possible to purify fractions of the prepituitary hormone to the extent that certain actions have been accentuated and others diminished; for example, an increase in thyrotropic, adrenotropic or gonadotropic action. Definite proof has been offered that the prepituitary hormone stimulates the gonads of both sexes but fails to act on the tubular apparatus of either sex directly. This signifies no action on the uterus and vagina in the female and on the seminal vesicles and prostate in the male. In other words, the prepituitary hormone produces no sexual effect on the castrate.

STEROID HORMONES

Gonadal.—Turning now to the hormones elaborated by the gonads, our knowledge is far more precise. In the female the ovary, through its granulosa cells, produces estradiol (dihydrotheelin) (1, fig. 1).[4] Estrone (theelin) (2, fig. 1) is found in the urine of pregnant women, mares and stallions. This well defined and extremely active chemical compound, 0.1 microgram (0.0001 mg.) being the international unit,[5] approximately the mouse unit, stimulates the uterus and vagina of the castrate, producing the now universally known effects. A close chemical relative of estrone elaborated by the corpus luteum (progesterone) continues the uterine effect (secretory) and causes the progestational changes necessary for embedding of the ova (3, fig. 1).

In the testes an allied chemical entity, testosterone (4, fig. 1), is elaborated. This acts on the prostate and seminal vesicles of the immature and castrate. Excretion is in the form of androsterone (5, fig. 1).

Adrenal.—Recently a masculinizing substance has been isolated from the adrenal cortex,[6] a substance likewise chemically closely related to the preceding.

Placental.—In addition, the placenta, a transient (gestational) gland of internal secretion, has been found to elaborate not only estrogenic and progesta-

From the gynecologic service and laboratories of the Mount Sinai Hospital.
Read before the joint meeting of the Chicago Medical Society and the Chicago Gynecological Society, Jan. 19, 1938.

1. Eppinger, H.; Falta, W., and Rudinger, C.: Ueber die Wechselwirkungen der Drüsen mit innerer Sekretion, Ztschr. f. klin. Med. **66**: 1, 1908.

2. Deanesly, Ruth, and Parkes, A. S.: Estrogenic Action of Compounds of the Androsterone-Testosterone Series, Brit. M. J. **1**: 257 (Feb. 6) 1936. Klein, M., and Parkes, A. S.: Progesterone-like Activity of Certain Male Hormone Compounds, Proc. Roy. Soc. London **121**: 574 (Feb. 3) 1937. Callow, R. K., and Parkes, A. S.: The Occurrence of Estrin and Progestin in Adrenal, Testis and Hypophysis, J. Physiol. **87**: 28 (March 14) 1936 (from Proceedings of the Physiological Society, March 14, 1936).

3. Van Dyke, H. B.: The Physiology and Pharmacology of the Pituitary Body, Chicago, University of Chicago Press, 1936.

4. MacCorquodale, D. W.; Thayer, S. A., and Doisy, E. A.: Isolation of Principal Estrogenic Substance from Liquor Folliculi, J. Biol. Chem. **115**: 435 (Sept.) 1936.

5. Doisy, E. A.: International Standard for the Ovarian Follicular Hormone, Science **77**: 344 (April 7) 1933.

6. Reichstein, T.: Ueber Bestandtheile der Nebennierenrinde: II. Adrenosterone, Helvet. chim. acta. **19**: 223 (March 16) 1936.

tional substances, identical with those produced by the ovaries, but likewise a prepituitary hormone, in many ways similar to that produced by the prepituitary.

CHEMICAL INTERRELATION

The close chemical resemblance of the estrogenic, androgenic and adrenogenic substances to one another and to cholesterol (6, fig. 1) favors the theory that cholesterol is the mother substance and that the gonads and adrenal cortex utilize this primary substance to elaborate their specific secretions. The possibility that, even at the primary site of elaboration, specificity is not absolute is brought up by the experiment of Hill,[7] who by transplanting the ovary to a cooler site (from the abdomen into the ear of the mouse) obtained restoration of the prostate and seminal vesicles in the castrate, a masculine reaction. This would signify that the ovary under these abnormal conditions secretes a male hormone. In the absence of the ovaries, estrogenic substances continue to be excreted in the female.[8] Where this is elaborated remains a mystery. It appears likely that at least some of the by-products or degradation products found during investigation of the body fluids and tissues, in sufficient concentration to produce physiologic reactions in test animals, play no role in the physiology of the body. But the regular presence of androgenic hormone in the female and estrogenic in the male cannot be side stepped by using this assumption. It is more probable that the chemically hermaphroditic conditions existing in the primate are as normal as the anatomically bisexual condition existing in the segments of Taenia, the common tapeworm. Much further study is required to clarify this question.

The question of bisexuality affects my own researches vitally because the conclusions drawn from the examination, qualitative and quantitative, of the estrogenic hormone found in the human circulation and human excretions may later prove to be so strongly altered by the discovery of antagonistic or additive action caused

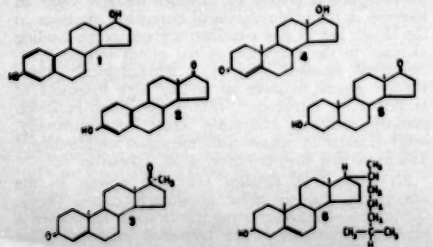

Fig. 1.—Structural formulas of steroid sex hormones and cholesterol. 1, estradiol, $C_{18}H_{24}O_2$, secreted by ovary. 2, estrone, $C_{18}H_{22}O_2$, excreted in urine. 3, progesterone, $C_{21}H_{30}O_2$, secreted by corpus luteum (excreted in urine as sodium pregnandiol glucuronidate). 4, testosterone, $C_{19}H_{28}O_2$, secreted by testis. 5, androsterone, $C_{19}H_{30}O_2$, excreted in urine. 6, cholesterol, $C_{27}H_{45}O$—C_8H_{17}, which may be the mother substance for all the steroid hormones.

by the presence of male hormones as to require complete or partial revision. The recent detailed studies of Gallagher, Peterson, Dorfman, Kenyon and Koch[9] are the first to supply reliable data for the daily excretion of both estrogenic and androgenic substances in normal and abnormal men and women. In both sexes surprisingly large amounts of the sexually opposite hormone occur—the average daily excretion of androgens is given by them as from 63 to 68 units for men and

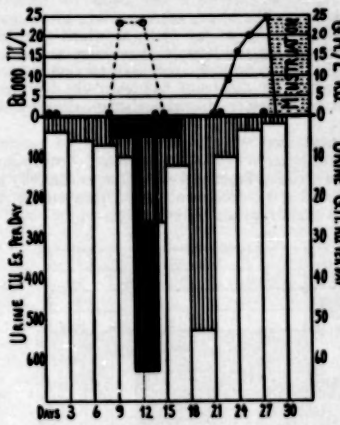

Fig. 2.—Estrogenic and gonadotropic assay in normal, fertile, menstruating women. Broken line and dotted circles, gonadotropic hormone in blood; black, gonadotropic hormone in urine; solid line and black dots, estrogen in blood; hatched lines, estrogen in urine. Normal urinary excretion of estrogens in twenty-eight to thirty day cycle equals 1,500 international units ±.

from 42 to 56 for women; of estrogens for men from 9 to 12 and for women from 18 to 36, the difference being most apparent in the estrogenic factor.

CLINICAL ASSAYS

After the discovery in 1925 of estrogenic hormone in the blood[10] and in 1927 in the urine,[11] clinical methods were developed for studying the concentration of these substances in normal women and in various conditions of disease. The technics employed are fairly standardized with the exception of a slight difference in interpreting the end reaction utilized by different investigators.

I shall give in briefest review such determinations as appear to have a direct clinical importance, particularly in controlling and evaluating the effects of therapy.

BLOOD AND URINE ASSAYS

Norms.—In my hands the fully normal, mature, fertile female shows surprisingly concordant hormonal conditions. The concentration of the estrogenic substance in the circulation remains low until the week preceding menstruation, attains its highest just before the menstrual flow begins and then rapidly diminishes. Estrogen is constantly excreted in the urine and feces throughout the cycle but around midperiod, corresponding to the time of ovulation, a marked increase of excretion persists for several days. The average level is

7. Hill, R. T.: Ovaries Secrete Male Hormone, Endocrinology **21**: 495 (July) 1937.

8. Frank, R. T.; Goldberger, M. A., and Salmon, U. J.: Estrogenic Substance in the Blood and Urine After Castration and the Menopause, Proc. Soc. Exper. Biol. & Med. **33**: 615 (Jan.) 1936.

9. (a) Gallagher, T. F.; Peterson, D. H.; Dorfman, R. I., and Kenyon, A. T.: Urinary Excretion of Estrogenic and Androgenic Substances by Normal Men and Women, J. Clin. Investigation **16**: 695 (Sept.) 1937. (b) Kenyon, A. T.; Gallagher, T. F.; Peterson, D. H.; Dorfman, R. I., and Koch, F. C.: The Urinary Excretion of Androgenic and Estrogenic Substances in Certain Endocrine States: Studies in Hypogonadism, Gynecomastia and Virilism, ibid. **16**: 705 (Sept.) 1937.

10. Loewe, Sigmund: Nachweis Brunsterzeugender Stoffe im weiblichen Blute, Klin. Wchnschr. **4**: 1407 (July 16) 1925. Frank, R. T.; Frank, M. L.; Gustavson, R. G., and Weyerts, W. W.: Demonstration of the Female Sex Hormone in the Circulating Blood: I. Preliminary Report, J. A. M. A. **85**: 510 (Aug. 15) 1925.

11. Aschheim, Selmar, and Zondek, Bernard: Hypophysenvorderlappen und Ovarialhormon im Harn von Schwangeren, Klin. Wchnschr. **6**: 1322 (July 9) 1927.

then resumed, to be followed by another still greater period of excretion, preceding menstruation by approximately three days and continuing until the first day of menstruation (fig. 2).

In the normal woman it has likewise been found that the gonadotropic substances show cyclic changes in the blood and urine. There is one period of increased accumulation in the blood, corresponding to the ninth to the eleventh day of the cycle, at which time both follicle stimulating and luteinizing reaction can be demonstrated. In the urine the period of maximum excretion is noted on the tenth and eleventh days, both gonadotropic factors likewise being demonstrated (fig. 2).

The next step was to study groups of carefully selected women who showed functional disturbances. The most striking functional disturbances clinically are the contrasting syndromes of amenorrhea on the one hand and menorrhagia or metrorrhagia on the other.

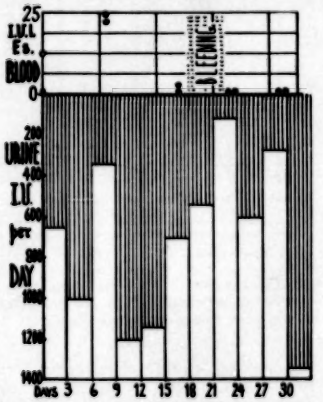

Fig. 3.—Assay in a case of menorrhagia and metrorrhagia. Total excretion of estrogens was 8,050 international units, 5½ times the normal.

Amenorrhea.—In amenorrheic patients it was found that at least three groups existed—one with absent or greatly diminished secretion and excretion of estrogens, another with absolutely normal estrogenic hormonal conditions, and a third in which the secretion and excretion, particularly the latter, were greatly increased. The simultaneous investigation of the gonadotropic status showed that these groups were present in some patients who had a completely normal gonadotropic cycle and others who showed no gonadotropic secretion or excretion. Provisionally one is forced to conclude that some additional factor, other than the gonadotropic and estrogenic, has escaped attention.[12] For reasons to be stated later, the uterus itself may be at fault, but a disturbance of the ratio femaleness : maleness might likewise produce amenorrhea. (Graphs of amenorrheic patients are given in a previous paper.[12])

The situation is hard to analyze, as the actual mechanism of menstruation is not fully understood, in spite of such light as has been shed by the researches of Barthelmez[13] on the structure and distribution of the endometrial vessels and by Markee,[14] who studied the endometrium transplanted into the anterior chamber of the eye, observing long periods of blanching—ischemia. The most generally accepted theory is that of deprivation of estrogen. As yet no proof whatever has been offered in substantiation of a "bleeding hormone," such as Hartman[15] and Kurzrok[16] assume.

Menorrhagia and Metrorrhagia.—Investigations of functional menorrhagias and metrorrhagias also have failed to clarify completely their causation. A few of the patients showed normal hormonal conditions of secretion and excretion. The majority of this group, however, were noted to have a marked increase in excretion of estrogens in the urine without a corresponding elevation of level in the blood (fig. 3). In one case of bleeding in puberty I have found the presence in considerable concentration of free estrogen in the urine.

My associates and I have regularly sought for this form of estrogen since Marrian[17] first directed attention to the fact that at various stages of pregnancy different quantities of combined (and therefore according to this author physiologically inactive or less active estrogen) and free ether soluble estrogenic substance were present. To the free estrogen he ascribed increased physiologic importance. The large number of nonpregnant women whom we have investigated from this standpoint, with the exception just mentioned, have shown entire absence or a minimal amount of the free estrogenic substance. Whether this as yet isolated observation will prove to have any importance requires further study.

As a group, functional menorrhagias and metrorrhagias give evidence of increased ovarian (estrogenic) activity without increased accumulation of estrogens or prepituitary hormones in the circulation.

Premenstrual "Tension."—The only condition, with the exception of pregnancy, in which we have found an increase in the accumulation of estrogenic substance in the blood, but in this condition without corresponding increase in the excretion, is the group termed "premenstrual tension" (fig. 4). Physiologically these women appear to have an unduly high threshold of excretion for estrogens. This is the group in which marked nervous symptoms occur premenstrually, relieved as if by magic with the onset of bleeding.[18] The menstrual flow, however, is not excessive.

Menopause.—A detailed study of women in the menopause, due to either physiologic causes (age), operative castration or x-ray sterilization, has shown a marked disturbance of the hormonal balance.[19] Our investigations were limited to the gonadotropic substance and estrogens. In the majority of these women, the gonadotropic substances are increased in both the blood and the urine and are continuously excreted.

12. Frank, R. T.; Goldberger, M. A.; Salmon, U. J., and Felshin, Gertrude: Amenorrhea: Its Causation and Treatment, J. A. M. A. **109**: 1863 (Dec. 4) 1937.

13. Bartelmez, G. W.: Histological Studies on the Menstruating Mucous Membrane of the Human Uterus, Am. J. Obst. & Gynec. **21**: 623 (May) 1931.

14. Markee, J. E.: Menstruation in Intra-Ocular Endometrial Implants in Macacus Mulatta, Anat. Rec. **64**: 32 (March 25) 1936.

15. Hartman, C. G.; Fitor, W. M., and Grilling, E. M. K.: The Anterior Lobe and Menstruation, Am. J. Physiol. **95**: 662 (Dec.) 1930.

16. Kurzrok, Raphael: The Endocrines in Obstetrics and Gynecology, Baltimore, Williams & Wilkins Company, 1937.

17. Cohen, S. L., and Marrian, G. F.: XIII. The Isolation and Identification of a Combined Form of Estriol in Human Pregnancy Urine, Biochem. J. **30**: 57 (Jan.) 1936. Cohen, S. L.; Marrian, G. F., and Odell, A. D.: CCCXIV. Estriolglucuronide, ibid. **30**: 2250 (Dec.) 1936.

18. Frank, R. T.: The Hormonal Causes of Premenstrual Tension, Arch. Neurol. & Psychiat. **26**: 1053 (Nov.) 1931.

19. Zondek, Bernard: Ueber die Hormone des Hypophysenvorderlappen, Klin. Wchnschr. **9**: 393 (March 1) 1930. Fluhmann, D. F.: Anterior Pituitary Hormone in the Blood of Women with Ovarian Deficiency, J. A. M. A. **93**: 672 (May 25) 1929.

This has been ascribed to overaction of the pituitary when unopposed by the ovaries. In many female castrates estrogens continue to be excreted for years.[8] As previously mentioned, the source of these estrogens has never been explained.

The response to estrogenic medication is accurately mirrored by the disappearance of the gonadotropic substances from the blood and urine during the time that this medication proves effective. This affords an accurate means of evaluating the success of the therapy quite apart from the subjective symptoms, previously the only available measure, which have led to so many discussions and disputes. The vaginal spreads obtained from these patients, as first recommended by Papanicolaou and Shorr,[20] likewise may offer some objective proof of the effect of therapy. We [21] have found the male hormone equally effective in abolishing the excess gonadotropic excretion and in relieving the subjective symptoms. The male hormone, however, requires larger dosage and appears to have no advantage over the female hormone.

Determination of Sex.—In spite of the presence of the female hormone in the male, the determination of sex in the presence of malformation as first advocated by us [22] in 1926 appears still to be of value, with the proviso that these determinations be continued over a sufficient length of time to show adequate periodicity. In the individuals investigated, recurring periodic peaks of estrogenic concentration in the blood and urine were noted at intervals of from twenty-one to twenty-five or thirty days in a given patient. No such periodicity has been described in the male.

Viability of Fetus.—Another valuable use for hormone assay is applicable to the determination of the viability of the fetus. In cases in which fetal death is suspected, viability can be decided in forty-eight hours. After the eighth week of pregnancy we [23] have regularly found at least 1 international unit of estrogen in 40 cc. of the woman's blood. Within twenty-four hours after the death of the fetus this level of concentration has diminished, giving a negative reaction.

Adrenal Carcinoma.—Finally an as yet unexplained hormonal condition has been noticed in the presence of adrenal cortical carcinoma.[24] In the four cases so far studied a mouse reaction was obtained with 2 cc., 1 cc. and, in one instance, as little as 0.075 cc. of straight urine, which signifies the presence of from 500 to more than 13,000 mouse units of estrogenic substance to the liter of urine in the presence of a negative pregnancy test. The estrogen test proved negative in cases of adrenal cortical hyperplasia, adenoma and other conditions producing syndromes similar to the adrenal cortical one but with absence of carcinoma of that gland.

Pregnancy Tests.—It is hardly necessary to emphasize the value or to describe the applications of the pregnancy tests. In our laboratory we employ the Friedman test exclusively both for normal and abnormal pregnancy and for the diagnosis of testicular tumors. In normal pregnancy we have noted a positive reaction with as little as 0.075 cc., although this is unusual and is considered a sign of abnormality (chorionepithelioma, hydatid) by some.

Whatever the future may have in store for the gonadotropic and estrogenic determinations, such as we perform, I can state without reservation that they have proved of great value to us in evaluating the various gynecologic and obstetric conditions which have confronted us in practice. They have helped us in diagnosis, in prognosis and in gaging the effects of therapy.

PROGESTIN ASSAY

Quite recently a new method of assay has been added to the armamentarium of the laboratory worker by Venning and Browne.[25] They have developed a gravimetric method for determining the amount of sodium pregnandiol glucuronidate excreted in the urine, which gives information as to when the corpus luteum begins to secrete, the amount secreted and how long the secretion persists. This affords an objective test to distinguish anovulatory from ovulatory menstruation and

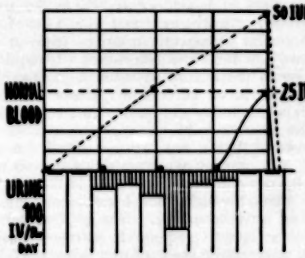

Fig. 4.—Assay in a case of premenstrual tension. Blood contained twice the normal amount of estrogens; urine excretion of estrogen, 320 international units, one fifth of normal excretion.

may serve also to show when progesterone is lacking during pregnancy and what clinical symptoms may be due to such lack.

Do these assays serve as a help and guide in treatment? It is apparent that cyclic variations in the concentration of gonadotropic, estrogenic and progestational substances occur in the blood of normal women. In amenorrhea the cycle may be absent, normal or decreased. In menorrhagia and metrorrhagia overproduction of estrogens with prompt excretion is the rule. In premenstrual tension overaccumulation of estrogens due to a high renal threshold is noted. In the menopause a continuous high level of gonadotropic factors exists in the blood. Are these known facts regarded in developing appropriate treatment?

THERAPY

The tendency to consider every obscure condition endocrine in origin is now in fashion. This tendency is so great that frequently no attempt is made to exclude nonendocrine disturbances; for example, in gynecology the disregard of fibromyomas of the uterus, incomplete abortion and even ectopic gestation as causes of bleed-

20. Papanicolaou, George, and Shorr, Ephraim: The Action of Ovarian Follicular Hormone in the Menopause, as Indicated by Vaginal Smears, Am. J. Obst. & Gynec. **31**:806 (May) 1936.

21. Salmon, U. J.: Effect of Testosterone Propionate upon Gonadotropic Hormones and Vaginal Smears of Human Female Castrates, Proc. Soc. Exper. Biol. & Med. **37**:488 (Dec.) 1937.

22. Frank, R. T., and Goldberger, M. A.: The Female Sex Hormone: V. A New Method of Determining Sex in the Presence of the Malformation of the Genital Organs, J. A. M. A. **87**:554 (Aug. 21) 1926.

23. Spielman, Frank; Goldberger, M. A., and Frank, R. T.: Hormone Diagnosis of Viability of Pregnancy, J. A. M. A. **101**:266 (July 22) 1933.

24. Frank, R. T.: A Suggested Test for Functional Cortical Adrenal Tumor, Proc. Soc. Exper. Biol. & Med. **31**:1204 (June) 1934; A Suggested Test for Cortical Adrenal Carcinoma, J. A. M. A. **109**:1121 (Oct. 2) 1937.

25. Venning, E. H., and Browne, J. S. L.: Studies on the Corpus Luteum Function: I. The Urinary Excretion of Sodium Pregnanediol Glucuronidate in the Human Menstrual Cycle, Endocrinology **21**:711 (Nov.) 1937.

ing. I have twice encountered patients who have received long continued courses of estrogenic treatment although they had no vaginas and minute solid rudimentary uteri, the anatomic cause of their amenorrhea never having been investigated or suspected. Similarly I have seen unmarried, amenorrheic patients treated with estrogens and thyroid extract for amenorrhea due to pregnancy, no physical examination having been performed.

In evaluating the results of therapy, one should take care likewise to exclude accidental or coincidental results, which are not uncommon. I have now ten patients in whom amenorrhea had persisted from two to seven years, who within four weeks of my first seeing them and without any therapy spontaneously menstruated. I have records also of a number of patients who conceived although amenorrheic for many years. I have been annoyed repeatedly during the hormonal study of patients with long continued menorrhagia or metrorrhagia to have their cycle become normal and continue normally, without medication having been given.

I must also warn against accepting with too much credence the reports of those authors who each year publish reports of wonderful results in the treatment of functional disturbances and the year following describe similar therapeutic triumphs with an entirely new remedy for the same disturbance. It requires little knowledge of the history of medicine to recollect the glowing reports of success by means of endocrine remedies which today are known to contain no active substances.

To instance but a few, let me recall the cure of vomiting of pregnancy in a large series of cases reported by a well known obstetrician [26] who injected a "corpus luteum" extract which later investigation showed to contain no active principle. Not so long ago hemophilia [27] was said to respond to estrogenic injections although more careful study proved this claim fallacious. Many must remember the claims made that any gonadotropic substance would cure baldness in either sex.[28]

Today a number of chemical entities are available; among the estrogenic substances are estrone, estradiol and its benzoate, estriol glucuronide (emmenin) available in strong concentration. The androgenic substances at our disposal are testosterone, testosterone propionate, androsterone and dihydroandrosterone benzoate. Progesterone, although the supply is limited, is likewise obtainable in pure form. In the prepituitary preparations, little standardization and little purification have been attained. Available are many extracts prepared from pregnancy urine; likewise, concentrates of the serum of pregnant mares, as well as growth and maturity factors derived from the prepituitary itself, all of which act on the laboratory animal but, at least in my hands, have as yet proved of little value when used in the human subject.

Were I to attempt to recount the application of these various substances on men and women, it would read too much like the prospectus of some pharmaceutical houses or the recommendations found in the majority of current endocrinologic manuals. However, in extenuation one should mention that the pamphlets sent out by the pharmaceutical trade, certainly those published by the more reliable firms, are based exclusively on clinical reports culled from medical literature.

Estrogens.—Recently estrogenic therapy has again been recommended in the treatment of nausea and vomiting of pregnancy. Hawkinson [29] reported forty-eight cures in fifty patients. The same type of treatment has been advocated by Schute [30] in eclampsia. Eight cases were studied. Throughout pregnancy huge quantities of estrogens are present in the blood stream; therefore this therapy appears illogical. No attempt as far as I know has as yet been made to treat the fetus in utero by these methods. However, Mabel Potter [31] found that premature infants responded to estrogens given by mouth, by general improvement and by added vitality. In the infant and adolescent, estrogenic vaginal suppositories containing 1,000 international units have helped to cure gonorrheal vaginitis by producing keratinization of the vagina and acidification of the vaginal secretion. Lewis and Adler [32] recently reported thirty cases of thirty-three cleared up in twenty days by this medication alone. Their results have been amply confirmed.

In the treatment of adults innumerable indications have been advocated. I shall mention such as are authenticated, even if in many instances I cannot agree with the results claimed.

Dysmenorrhea, that debatable field, the causation of which has never been fully clarified, according to Novak,[33] responds to estrogenic therapy given between the periods. Lackner, Krohn and Soskin [34] would limit its use to patients with dysmenorrhea whose uteri are small and infantile. In amenorrhea, most authors have recommended the estrogens. Kurzrok, Wilson and Cassidy [35] found that large doses are required. With this I can fully agree, although the therapy to me appears futile. In fact, the difference in response between functional amenorrhea and the amenorrhea noted in the menopause is so striking that I utilize it in diagnosis.[12]

Not infrequently one encounters women in the late thirties and the question arises whether one is dealing with a premature menopause or a transient functional amenorrhea. In addition to the finding that the menopausal patients show a continuous high excretion of gonadotropic factor in the urine, they respond to as little as 150,000 international units of estrogen by disappearance of the gonadotropic factor in their excretion and, after withdrawal, not infrequently by the appearance of uterine bleeding. To induce uterine bleeding in functional amenorrhea requires at least 1,000,000 international units.

I have seen no permanent improvement in amenorrhea resulting from estrogenic medication. The rare condition of premenstrual edema appearing in the face and hands, sometimes widespread over the entire body, may be relieved by giving emmenin, the estriol glucuro-

26. Hirst, J. C.: Corpus Luteum Extract in Nausea of Pregnancy, J. A. M. A. **66**:645 (Feb. 26) 1916.

27. Birch, Carroll L.: Hemophilia and the Female Sex Hormone, J. A. M. A. **97**:244 (July 25) 1931.

28. Brengton, B. N.: Prepituitary Alopecia, J. A. M. A. **97**:1355 (Nov. 7) 1931.

29. Hawkinson, L. F.: Nausea and Vomiting of Pregnancy: Fifty Cases Treated with Estrogenic Preparations, Minnesota Med. **19**:519 (Aug.) 1936.

30. Schute, Evan: The Use of Estrin in the Treatment of Eclampsia, Endocrinology **21**:594 (Sept.) 1937.

31. Potter, Mabel F.: Estrogenic Substance Used in the Treatment of Premature Infants, Brit. M. J. **1**:1201 (June 12) 1937.

32. Lewis, R. M., and Adler, E. L.: Endocrine Treatment of Vaginitis, J. A. M. A. **106**:2054 (June 13) 1936.

33. Novak, Emil: The Treatment of Primary Dysmenorrhea with Especial Reference to Organotherapy, Am. J. M. Sc. **185**:237 (Feb.) 1933.

34. Lackner, J. E.; Krohn, Leon, and Soskin, Samuel: The Etiology and Treatment of Primary Dysmenorrhea, Am. J. Obst. & Gynec. **34**:248 (Aug.) 1937.

35. Kurzrok, Raphael; Wilson, Leo, and Cassidy, M. A.: The Treatment of Amenorrhea with Large Doses of Estrogenic Hormone, Am. J. Obst. & Gynec. **29**:771 (June) 1935.

nide, discovered by Collip [36] and purified by Marrian.[37] In this I can agree fully with Atkinson and Ivy.[38]

Riley, Brickner and Kurzrok [39] have used estrogens in a dosage of 50,000 international units for the treatment of premenstrual migraine. My own experience has not been as favorable as theirs. Migraine, like dysmenorrhea, is as yet a very loose concept ascribable to many causes and ill defined.

The relief of painful breasts and adenosis, according to Lewis and Geshickter,[40] may be obtained by long continued treatment with estrogens. In the great majority of patients the pain is self limited and clears up spontaneously within two to six months. I would therefore regard therapeutic results with reserve if the condition is of short duration. In two instances in which the symptoms persisted for years, complete restoration to the normal occurred after pregnancy and lactation. However, I can hardly advise this as a regular therapeutic measure.

Among the more recent therapeutic uses of estrogens, their application has been recommended in the treatment of acne in both sexes,[41] in atrophic rhinitis [42] and in "Cushing's syndrome," [43] which would include the more frequent adrenal cortical syndrome. Their use has likewise been advocated in hirsutism in the female, presumably to counteract the presence of a masculinizing factor. These reports require further confirmation.

The neurovascular, digestive and many of the other disturbances of the menopause are promptly relieved by sufficient doses of estrogens. Severinghaus [44] was the first one to give adequate amounts. This in my opinion is the sovereign field for the use of estrogens. The flushes, sweats, psychic unrest, indigestion, arthritic symptoms and vaginitis of the menopause promptly disappear. The therapy may be given parenterally (hypodermically in oily medium) or by mouth (progynon-DH [estradiol]). The dosage necessary varies between 100,000 and 150,000 international units in the course of two weeks. A return of flushes requires resumption of this therapy, usually at increasingly long intervals. Withdrawal of the medication is frequently followed by uterine bleeding, even in the aged, and need occasion no disquiet.

As indicated from the foregoing, senile vaginitis responds likewise to estrogenic therapy.[45] Transient improvement may be expected in kraurosis vulvae, but I consider the therapy, after many years of trial, purely palliative because of the frequent recurrences of itching, the unarrested progression of atrophy and the appearance of carcinoma in kraurotic areas. Vulvectomy is far preferable to long continued treatment by estrogens.

As could be anticipated from the effect on the milder nervous symptoms of the menopause, it is not surprising that glowing reports of the benefit exerted on involutional melancholia and the menopause psychoses have been published.[46] The dosage advocated has varied between 5,000 international units twice a week and from 150,000 to 200,000 international units a month.

I do not consider the reports on the treatment of sterility and of menorrhagia by means of estrogen of sufficient importance to warrant more than passing mention.

The question has been raised whether estrogenic medication may favor carcinogenesis. No direct confirmatory evidence has been adduced in the human being. With so much cholesterol and intermediate cholesterol derivatives normally circulating in the blood, no such by-effects need be anticipated from enteral or parenteral absorption, with the reservation that localized dermal applications should be avoided, as the skin is particularly responsive to continued application of or exposure to carcinogenic agents in both animals and human beings.

Corpus Luteum Hormone.—The corpus luteum hormone has proved of distinct value in two conditions. It is available in the form of a crystalline product, progesterone, usually now of synthetic derivation.

It has been recommended for dysmenorrhea by Wilson and Elden.[47] They found that it afforded relief in 59 per cent of seventeen cases. Their dosage was from one fifth to 1 international (Corner) unit, given from three to six days before the onset of the anticipated period. I have reserved this treatment for the most intractable cases, which have resisted all other therapy and in which castration or presacral sympathectomy had been advised by others. The dosage that I employ is 1 rabbit unit on successive days, starting three days before the anticipated period, and 5 rabbit units morning and evening on the day preceding, sometimes also on the first day of menstruation. Its effect in these cases has been satisfactory.

Another use for progesterone has been found in threatened and habitual abortion. Here the criteria available in judging its efficacy are difficult to formulate. Falls, Lackner and Krohn [48] have reported thirty-four successes among forty-one cases. Numerous other reports are available. My own experience is comparatively small. I can state that, in two cases in which four successive abortions had occurred previously, pregnancies ran an uninterrupted and successful course. In numerous other patients with one to two antecedent abortions, the accidental factor has been too great to permit of valid deductions. Here the Venning [49] test may prove an aid in controlling clinical application.

Prepituitary and Prepituitary-like Therapy.—Three different types of therapeutic agents must be considered. Gland substance itself, not available in sufficient quantity or concentration; concentrated serum of pregnant mares, which is just becoming available in higher concentration, and the readily obtainable anterior pituitary-like factor derived from pregnancy urine.

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My own experience agrees with the recent report of Hamblen and Ross [50] that there is no response in the human ovary to subcutaneous injections of anterior pituitary-like factor. Its use has been advocated in dysmenorrhea by Novak [51] in 1933; in functional bleeding, by Novak and Hurd,[51] Henderson [52] and Wilson and Kurzrok,[53] the latter also combining it with extract of corpus luteum. I can in no way agree with their observations.

This therapy has been advocated for amenorrhea by many authors.[54] Anterior pituitary-like gonadotropic factor has proved entirely ineffective in my hands no matter what the dosage used. I am now trying the Upjohn preparation (not on the market) and also the Danish Antex-Leo, both from pregnant mare's serum, for amenorrhea but am not ready to report finally, although the results are not encouraging.

Davis in the discussion of a paper and also in the discussion of my present presentation has informed me that he injects the concentrate of pregnant mare's serum intravenously in the human being. Ovulation and corpus luteum formation take place. From other as yet unpublished results I gather that ovulation can be induced not only in normal but also in amenorrheic and sterile patients. Severe allergic symptoms—shock, serum sickness, and the like—are bound to occur unless great caution is used. I myself have not had the temerity to use this preparation intravenously.

The use of anterior pituitary-like gonadotropic factor in undescended testicle has proved a boon, although the results obtained are not as uniform as they were at first asserted to be. In diagnosing undescended testes one should take care not to include a testicle drawn up high in the scrotum against the external inguinal ring, or, if this is large, even within the canal. A warm bath will show whether the testis is really undescended. Schapiro [55] in 1930 first introduced this method of therapy. It has been utilized by Goldman and Stern,[56] Lawrence and Harrison [57] and many others. Today long continued injections rather than huge doses are advised. From 100 to 300 rat units given twice a week over several months will show whether in a given case this therapy proves effective. In every instance one should use it before resorting to surgery.

A single large dose (1,200 rat units) may be of use in determining the site of an intra-abdominal testicle, as this high dosage usually produces well localized pain corresponding to the location of the undescended testis.

The use of anterior pituitary-like gonadotropic factor in hypogonadism, over long periods of time, has been advocated by the majority of endocrinologists. The good results reported, in my opinion, are due to a misconception. The patients in this numerous group, which includes mainly boys between 12 and 15, obese, delicate skinned, with poorly marked secondary sex characteristics, small phallus and gonads, in the large majority are suffering from a self-limited retardation. Fully 90 per cent of these adolescents become normal without therapy but at an age later than that of the majority of normal boys. The therapy, if continued for several years, is therefore credited with their improvement. In the older age group no improvement is noted. McCahey, Hansen and Soloway [58] noted no increase in excretion of male hormone in five cases of hypopituitary hypogonadism in which 200 rat units of this substance was given twice a week.

I am not able to give my personal evaluation of the efficacy of anterior pituitary-like gonadotropic factor in azoospermia,[59] male sterility [60] and impotence. These reports are not convincing, as careful and long continued counting of the spermatozoa before and after treatment is needed.

The application of anterior pituitary-like gonadotropic factor in both males and females suffering from Fröhlich's disease has been reported.[61] In my own hands the effect has been nil. The same applies to an even greater degree in the treatment of Simmonds' disease, a condition in which the pituitary has lost its function and which is as fatal as Addison's disease. Good reports have been published by Hicks and Hone,[62] Hawkinson [63] and Dunn.[64] I agree with Regester and Cuttle,[65] who tried the anterior pituitary-like gonadotropic factor, the growth factor and also the maturity factor without avail.

It should be remembered that there is at least one syndrome, particularly common in adolescents, which imitates Simmonds' disease in the most striking fashion. It is sometimes called "anorexia nervosa" and is based entirely on psychic factors, often produced by voluntary, secret starvation. This condition, which I have repeatedly seen diagnosed as Simmonds' disease, responds magically to separation from the family and elucidation of the underlying psychic cause.[66]

Some of the other uses of anterior pituitary-like gonadotropic factor which appear to be based on a most insecure foundation and do not require discussion are the treatment of acne,[67] hyperthyroidism [68] and even enuresis.

Male Sex Hormones.—The male sex hormones available for therapeutic use are testosterone and testosterone propionate, dihydroandrosterone benzoate as well as androsterone. It is only recently that really accurate titrations of the amount of male and female sex hor-

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65. Regester, R. P., and Cuttle, T. D.: Cachexia Hypophyseopriva (Simmonds' Disease), Endocrinology **21**:558 (July) 1937.

66. Moschcowitz, Eli: Anorexia Nervosa, Anniversary Volume for Robert Tilden Frank, St. Louis, C. V. Mosby Company, 1937, p. 359.

67. Lawrence, C. H.: The Anterior Pituitary-like Hormone: A Clinical Study of Its Effects in Acne Vulgaris, J. A. M. A. **106**:983 (March 21) 1936.

68. Starr, Paul, and Patton, Helen: Sex Hormone Treatment of Hyperthyroidism, Endocrinology **18**:115 (Jan.-Feb.) 1934.

mone found in normal [68] and in diseased males [69] have become available, and therefore as yet the results recorded are based on purely empirical evidence. Those permitting of any critical evaluation are surprisingly few.

The McCullaghs and Hicken [69] report improvement of neurovascular symptoms and some return of libido in castrates treated with androtin, containing only 6 capon units per injection. Our own attempts to treat the two castrates available to us were handicapped by the fact that the one suffered from no symptoms and in the other one, a case of bilateral tuberculosis, an acute pulmonary lesion developed which definitely interfered with the evaluation of criteria. The marked excess of gonadotropic substance in the urine was unaffected by doses of androsterone (20 mg.), dihydroandrosterone benzoate (25 mg.) and testosterone (115 mg.), nor was estrogenic therapy, which proved so effective in the female castrate,[8] of any avail.

This is particularly surprising, since testosterone and testosterone propionate cause the gonadotropic hormone to disappear in the female castrate [21] and relieve the symptoms in a fashion identical with that of the estrogens, although large doses are required.

The reports on rejuvenation experiments are not directly applicable to this discussion, since they consist largely of transplantation, sometimes of heterologous testicular tissue or of ligation of the vas. The testicular "mush" injected by Stanley [70] likewise does not allow of any critical review. The few reports on the treatment of azoospermia with androgens are entirely unconvincing. McCullagh and Hicken [69] report improvement in hypogonadism with the same preparation they used in eunuchs.

Considerable literature has accumulated on the treatment of enlargement of the prostate by means of androgens. After castration and in hypogonadism, the size of the prostate is diminished. Prostatic enlargement is a change noted increasingly with advancing age. It has been ascribed to lack of male hormone. However, in experiments, injections of androgen into castrates increase the size of the prostate. The question is further complicated by the reports of Deming,[71] who states that a large number of prostatic enlargements arise from the submucous glands and that these structures are uninfluenced by endocrine stimuli. With these numerous inconsistencies to be accounted for, the published results require the strictest scrutiny.

Van Cappellen [72] in 1933 reported improvement in prostatic hypertrophy following the injection of an androgen called Hombreol. Eleven of twelve patients were said to have shown marked improvement. Since then Laqueur [73] has collected 127 cases, mainly from the literature, and likewise records improvement. Another report, by Gostimirović,[74] describes four of thirteen cases markedly improved in which from 272 to 1,182 capon units in the total treatment was used. This report, as well as the preceding ones, is not convincing, as the criteria are subjective. Similar results are claimed by Day, Martin, Kutzmann and Kessler,[75] who note improvement in forty patients with prostatic hypertrophy treated with testosterone. In none of these quoted articles has any real measurement of the prostate either by rectal palpation or by cystoscopy been attempted, the subjective symptoms alone being evaluated. Lower [76] has employed preparations which he calls "Inhibin" as well as "Contruin." From Lower's description as well as from the names he has given to the preparations, it would appear that he ascribes the effect to a purely hypothetical antihormonal action. As I have refrained throughout my discussion from trenching on the very debatable subject of antihormones, I shall certainly not take it up in this connection. The results obtained by Lower and his group are likewise impossible to evaluate.

I may therefore state that male hormone therapy is just beginning. Every effort should be made to obtain comparable clinical criteria. In the eunuch the disappearance of the excess excretion of gonadotropic hormone is a strictly objective criterion. Definite return of libido is confirmatory evidence, as this is said to disappear in 90 per cent of the cases, according to the most recent German statistics,[77] a country in which a large number of castrations have been performed. Complete disappearance of the neurovascular symptoms, if present, can be utilized in the same fashion. Needless to say, treatment will be purely palliative as in the female. In hypogonadism I see no prospect of androgenic hormone therapy correcting the condition, which must be ascribed primarily to prepituitary deficiency. Whether the treatment will prove of real value in azoospermia and prostatic hypertrophy appears today to be an open question.[78]

CONCLUSIONS

1. The sex hormones consist of two groups:

(*a*) The prepituitary (adenohypophysis) and prepituitary-like (A. P. L., placenta, pregnancy urine).

(*b*) The steroid hormones (ovary, testis, adrenal, placenta).

2. The prepituitary and prepituitary-like hormones are of protein composition; their structure is unknown; they act on the ovary and testis.

3. The steroid hormones have been isolated; their structure has been determined; they act on the müllerian and wolffian ducts in the immature, adult and castrate subject.

4. A permanent condition of chemical hermaphroditism persists throughout life in the human male and female. Disturbances in the ratio maleness: femaleness may perhaps give rise to clinical manifestations.

5. Absence, decrease or increase of the estrogens and/or of progestin causes functional disturbances in the female. Functional disturbances in the male, as yet not as well defined, are probably due to similar variations of androgen secretion.

6. The exact chemical constitution of active estrogens and androgens which occur in the circulation have not been fully clarified. Combinations, intermediate products and products in process of excretion have different potencies. These variations as yet defy analysis.

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73. Laqueur, Ernst: Treatment of Prostatic Hypertrophy with Male Hormone (Hombreol) and Experimental Foundation of This Therapy, Schweiz. med. Wchnschr. **64**: 1116 (Dec. 8) 1934.
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75. Day, R. V.; Martin, H. W.; Kutzmann, A. A., and Kessler, E. E.: Sex Hormone Therapy for Prostatism, Am. J. Surg. **39**: 100 (Jan.) 1938.
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7. The steroid sex hormones when given in small amount and for short periods stimulate prepituitary function; in large amount and over longer periods of time they inhibit it.

8. In the female, estrogens are of use in the treatment of infantile gonorrhea and in almost every variety of menopause disturbance. Estrogens have been employed in many other conditions without convincing evidence of their efficacy. Progestin relieves dysmenorrhea and may prevent abortion due to defective function of the corpus luteum of pregnancy.

9. Androgens should prove effective in the relief of castration symptoms in the male. They are being tried for many other diseases.

10. Anterior pituitary-like gonadotropic factor is effective in causing the descent of the testis in a large percentage of bilateral and unilateral cryptorchid patients.

11. When direct endocrine therapy is unavailing, improvement or cure may yet be obtained by other measures such as snake venom, curettage or roentgen therapy for menorrhagia; protein diet, reduction of obesity or thyroid extract for amenorrhea.

12. There is every prospect that when our understanding of the complicated hormone conditions which confront the endocrinologist are further clarified and when prepituitary preparations are improved, the therapeutic results will be bettered.

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OXYGEN IN HIGH CONCENTRATIONS FOR RELIEF OF PAIN

IN CORONARY THROMBOSIS AND SEVERE ANGINA PECTORIS

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LOS ANGELES

There are two immediate objectives in the treatment of patients with acute coronary thrombosis, namely the support of the circulation and the relief of pain. The beneficial effects of oxygen administration in sustaining cardiorespiratory function, especially when significant degrees of shock or pulmonary edema exist, are well known. It is not widely recognized, however, that the inhalation of oxygen in high concentrations is effective in alleviating the pain associated with coronary thrombosis and angina pectoris.

The pain associated with coronary thrombosis is notoriously variable in intensity. Its severity depends on the size of the coronary artery occluded, the speed of occlusion, the adequacy of coronary arterial anastomoses, the activity to which the myocardium is subjected, the sensitivity of the patient to pain, and other factors. Pain may be entirely absent [1] or so mild that the underlying pathologic state is overlooked. In the vast majority of instances it is adequately controlled by the administration of morphine or other derivatives of opium. Oxygen in these cases is unnecessary unless symptoms of cardiorespiratory impairment are present. Occasionally, however, the pain accompanying a sudden major arterial occlusion is so extreme that even large doses of opiates fail to control it. The employment of oxygen at concentrations of from 80 to 100 per cent in such cases becomes an important therapeutic adjunct.

A parallelism exists in cases of coronary sclerosis with angina pectoris. In many instances the pain is sufficiently controlled by the restriction of activity alone. In others the addition of sedatives, perhaps in combination with one of the xanthine derivatives, seemingly modifies the frequency and severity of the seizures to a degree sufficient to afford relative comfort. Rarely is the pain so severe that glyceryl trinitrate in proper dosage fails to give symptomatic relief. Extreme cases, however, are encountered in which paroxysms are occasioned by the slightest exertion or excitement. Under such circumstances the usual medication may be inadequate to control the discomfort or administration of glyceryl trinitrate may be necessitated too often to be a safe procedure. The employment of oxygen in high concentrations in such instances may afford considerable comfort to the patient.

Rizer,[2] employing the tent apparatus in 1929, noted that the pain resulting from acute coronary thrombosis could be relieved by inhalation of oxygen. This observation was subsequently confirmed by Barach,[3] Barach and Levy [4] and others.[5] Mild or moderately severe pain often may be alleviated when the oxygen tent is used. In my experience, relief from severe pain is seldom complete when oxygen is employed in concentrations of from 40 to 60 per cent such as are afforded by a well regulated tent apparatus. Dramatic abatement of pain, however, may be produced by the administration of oxygen in high concentrations (from 80 to 100 per cent). Efficient continuous administration of oxygen at such concentrations has recently been made possible by an inhalation apparatus designed by Boothby, Lovelace and Bulbulian. The B. L. B. mask has been fully described and its clinical uses outlined by Lovelace.[6] It served as a simple, comfortable and economical method of oxygen administration in the cases to be reported.

ILLUSTRATIVE CASES

Case 1.—A merchant aged 62, first seen Oct. 15, 1938, had been conscious of a cardiac irregularity for twenty-eight years. For three months he had noted, on exertion, a sense of retrosternal pressure which was entirely relieved by rest. Electrocardiographic tracings failed to reveal evidence of myocardial degeneration. A diagnosis of coronary sclerosis with angina pectoris was made.

While at rest October 18 the patient was seized with an excruciating retrosternal pain which radiated to the left shoulder and elbow. The pain was accompanied by moderate dyspnea and by symptoms of mild shock. One grain (0.065 Gm.) of morphine sulfate administered in doses of one fourth grain (0.016 Gm.) within a period of one and one-half hours failed to provide relief. One hundred per cent oxygen was then administered by means of a B. L. B. apparatus; within three minutes the pain ceased. The apprehension, restlessness and dyspnea subsided and the patient fell asleep. For the ensuing twelve hours 100 per cent oxygen was administered continuously. When an attempt was made to discontinue its administration the pain recurred. Relief was obtained promptly when oxygen

From the Medical Service, St. Vincent's Hospital, and from the Department of Medicine, University of Southern California School of Medicine.

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2. Rizer, R. I.: Oxygen in Treatment of Coronary Occlusion: Preliminary Report, Minnesota Med. **12**: 506-507 (Aug.) 1929.

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therapy was reinstituted. During the succeeding five days oxygen was employed continuously except for short interruptions every three or four hours. Retrosternal pain almost invariably recurred when the inhalation was interrupted and on three occasions there were severe exacerbations. Each of these promptly subsided when treatment was resumed. Electrocardiographic studies made on the fourth day disclosed the characteristic manifestations of a posterior basal infarction.

Six days after the onset, oxygen therapy was discontinued and episodes of paroxysmal ventricular tachycardia, lasting from ten minutes to several hours, made their appearance. Quinidine sulfate was tried in doses up to 30 grains daily for five days but without effect on either the frequency or the duration of the attacks. At the suggestion of the patient, oxygen administration (100 per cent) was again tried. Subsequent episodes of tachycardia were aborted in from two to ten minutes with inhalations of oxygen. Recovery otherwise was uneventful.

Complete relief of intense pain accompanying coronary thrombosis was obtained in case 1 by the administration of 100 per cent oxygen. Large doses of morphine had failed to afford relief. Except for brief interruptions, 100 per cent oxygen was inhaled for five days without signs of pulmonary irritation. It is interesting that 100 per cent oxygen invariably aborted the attacks of paroxysmal ventricular tachycardia when quinidine therapy had failed. The therapeutic implication arising from this observation is obvious.

CASE 2.—A rancher aged 67, first observed July 16, 1938, had six hours previously, while eating, suddenly experienced dyspnea and a "constricting pain" in the left side of the chest. The pain became increasingly more severe and was accompanied by symptoms of mild shock. Two hours later one-half grain (0.03 Gm.) of morphine sulfate was administered with marked relief. He remained relatively comfortable and almost free from pain for two days. July 18, while using the bed pan, he was seized with excruciating retrosternal pain. Morphine sulfate, one-fourth grain, gave only partial relief. Marked dyspnea and symptoms of shock supervened. Oxygen (100 per cent) was employed by means of a B. L. B. mask. The striking reduction of pain and subsidence of dyspnea which followed were impressive. Oxygen was utilized for eight hours and then interrupted without recurrence of pain. Four similar attacks took place during the next two days when the patient attempted to use the bed pan. Each time the pain was alleviated almost immediately by 100 per cent oxygen. A B. L. B. mask was applied before the patient was allowed to use the bed pan during the next ten days. No further episodes ensued. Recovery otherwise was uneventful. Electrocardiographic tracings taken on the fourth day disclosed a posterior basal infarction.

The immediate subsidence of pain following the administration of oxygen was striking. Further, the prophylactic application of oxygen before necessary slight effort was permitted appears to have prevented the recurrence of pain and shock.

CASE 3.—A man aged 72, examined Nov. 12, 1938, had for one year noted dyspnea on effort. November 2 he had experienced a dull ache in both pectoral regions, the right shoulder and both elbows. This episode had lasted two hours. The following day he traveled 500 miles by airplane and felt no discomfort. During the four days prior to observation he experienced four attacks of bilateral pectoral pain with radiation to both elbows. November 11 a persistent aching pain developed in both elbows. During the night it became increasingly more severe and by morning intense pain was present in both pectoral regions and the elbows. The patient was brought directly to the hospital. No medication was administered. Complete relief of pain was induced by the administration of oxygen (100 per cent) by means of a B. L. B. mask. One hundred per cent oxygen was given continuously for two days, except for brief interruptions every three to four hours. Pain almost invariably recurred when the oxygen was interrupted but was promptly relieved when the treatment was resumed. For three days, from 50 to 60 per cent oxygen was given continuously and then discontinued without recurrence of pain. Electrocardiographic tracings on the fifth day disclosed the typical manifestations of a posterior basal infarction. The patient's progress was satisfactory until the fifteenth day, when a cerebral vascular accident with a resultant right hemiplegia occurred. Paralysis of the right arm and leg persists to date.

Case 3 illustrates the alleviation of intense pain by the administration of oxygen alone. Opiates were not used in the treatment of this patient.

CASE 4.—A mining engineer aged 64 had experienced no cardiac symptoms prior to the present illness. During a business conference Sept. 6, 1938, he was seized with a severe retrosternal pain which radiated into both pectoral regions and which was accompanied by symptoms of mild shock. One-fourth grain of morphine sulfate was administered prior to hospitalization, with slight relief. The injection was followed by protracted vomiting. The patient was placed in an oxygen tent with the concentration of oxygen at approximately 50 per cent. No relief of pain was obtained. The enclosure worried the patient and augmented his restlessness. One-third grain (0.02 Gm.) of pantopon (hydrochlorides of the alkaloids of opium, principally morphine) was given and was followed by nausea, protracted vomiting, accentuation of the pain and a greater degree of shock. The B. L. B. mask was applied with the oxygen concentration at 100 per cent. The relief of pain as well as the cessation of nausea, vomiting, dyspnea and shock occurred within fifteen minutes. Oxygen was administered constantly for forty-eight hours, except for brief intervals of from ten to fifteen minutes every three hours. He remained surprisingly comfortable during this time. On the second day a gallop rhythm, best heard over the apex, was noted. On the third day the apex rate fell to twenty-eight beats a minute. An electrocardiogram disclosed a complete auriculoventricular block together with the characteristic manifestations of a recent coronary thrombosis. In spite of continuous oxygen administration sudden circulatory collapse ensued and the patient died on the third day. Permission for necropsy was not obtained.

Case 4 illustrates the relief of pain with 100 per cent oxygen when administration of oxygen in a lesser concentration by means of the tent had failed. The exertion provoked by the protracted vomiting following the administration of morphine and pantopon may have contributed toward the fatal outcome.

CASE 5.—A minister aged 62 had suffered with angina pectoris for nine years. In the beginning the attacks were mild and consisted of a sense of choking accompanied by dyspnea on moderate exertion. Gradually the character of sensation changed to that of retrosternal pressure and later to a "viselike" constriction behind the sternum. The attacks were always precipitated by effort or excitement, lasted from one to ten minutes and were invariably relieved by rest. Occasionally the retrosternal distress was accompanied by pain in the left shoulder and elbow. Glyceryl trinitrate in doses of one one-hundredth grain (0.65 mg.) was always effective in affording relief. Fourteen months prior to observation he had been confined to bed for a period of seven weeks because of suspected coronary thrombosis. Electrocardiograms taken at that time showed definite T wave changes in leads 1 and 2 but were not conclusive for recent coronary thrombosis. For one year prior to observation the attacks of anginal pain became progressively more severe and were provoked by less effort or excitement. Though several attacks had lasted for as long as fifteen or thirty minutes, the majority were of less than ten minutes' duration.

When the patient was first seen, Jan. 4, 1939, he was confined to bed because even slight exertion or excitement occasioned severe anginal pain. He preferred to stay absolutely quiet in bed rather than take the repeated doses of glyceryl trinitrate necessary to permit even slight activity. Such trivial acts as shaving, eating, listening to an exciting radio program, bending to tie a shoe lace or defecation would incite a painful paroxysm. A B. L. B. oxygen apparatus was installed at the patient's bedside. Inhalation of 100 per cent oxygen brought either complete

relief or marked amelioration of the distress. The relief was more prompt and more complete than that afforded by glyceryl trinitrate and was unaccompanied by the unpleasant symptoms induced by the drug. Application of the mask prior to the execution of minor activities known to produce anginal pain served to prevent the paroxysms.

Angina pectoris of this severity offers a distressing problem to both the patient and the physician. Paravertebral injection of alcohol was considered, but the procedure was refused by the patient. Sympathectomy was not urged because of the uncertainty of results and the relatively high mortality attending the operation in patients of his age. The administration of oxygen in high concentration added materially to the patient's comfort. Its use is to be recommended in similar cases presenting the extreme anginal syndrome.

COMMENT

Recently the mechanical theory of the origin of coronary pain advocated by Wenckebach[7] has been reawakened by Herrmann[8] and by Martin and Gorham.[9] The majority of clinicians, however, adhere to the ischemic or anoxemic concept.[10] According to the ischemic theory, impaired coronary circulation results in anoxemia of the myocardium and the accumulation of metabolites. These substances, particularly lactic acid, chemically irritate the perceptors of the sympathetic afferent nerves with the reflex production of pain. The cessation of pain following the inhalation of 100 per cent oxygen in the cases reported lends further support to the anoxemic theory. Boothby[11] has pointed out that the administration of pure oxygen increases the oxygen content of arterial blood by from 10 to 15 volumes per cent. In cases of coronary thrombosis the myocardial anoxemia is evidently partially overcome by the delivery of hyperoxygenated blood through the collateral coronary circulation. In cases of coronary sclerosis with angina pectoris the mechanism is obvious.

The prompt relief of pain in each case of coronary thrombosis reported was dramatic. Relief was obtained within ten minutes after oxygen therapy was instituted. Invariably the apprehension, restlessness and dyspnea and the symptoms of mild shock were quickly controlled. The administration of 100 per cent oxygen is advocated when the pain is intense or is resistant to opiates.

Pulmonary irritation and even pneumonia have been produced in animals by the continuous inhalation of mixtures containing more than 70 per cent oxygen.[3] For this reason many clinicians have discouraged the use of highly concentrated oxygen except for brief periods. I have noted no cases of pulmonary irritation in which 100 per cent oxygen has been employed. Interruption in oxygen therapy for from ten to fifteen minutes every three to four hours has been made in each case in order to prevent the possibility of pulmonary irritation. Boothby, Mayo and Lovelace[12] have recently reported the administration of 100 per cent oxygen to more than 800 patients without observing the slightest evidence of pulmonary irritation. In the majority of their cases oxygen in this concentration was not administered continuously for more than forty-eight hours.

CONCLUSIONS

The administration of oxygen in high concentrations serves as an efficient method of relieving the intense pain which may accompany acute coronary thrombosis and as an important therapeutic adjunct in the symtomatic control of severe angina pectoris.

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CONGENITAL ABSENCE OF THE GALLBLADDER

WITH PRIMARY CARCINOMA OF THE COMMON DUCT AND CARCINOMA OF THE LIVER

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Congenital anomalies of the liver and gallbladder are relatively rare. The importance of these structural defects is such that it is hoped more attentive observation will be directed toward them. A survey of the literature reveals ninety-six cases of congenital absence of the gallbladder, and this is frequently associated with stenosis and absence of the hepatic and common ducts. These anomalies are by no means incompatible with life. Normal liver function may be maintained under these anatomic handicaps.

Observations During First Admission

Date	9/5/37	9/6/37	9/7/37
Urine	Neg.	.....	Neg.
Hemoglobin	80%	80%	
Red blood cells	4.72	4.78	
White blood cells	20,600	10,200	
Polymorphonuclears	82%	82%	
Lymphocytes	18%	18%	
Mononuclears	....	2%	
Blood Wassermann and Kline reactions	....	....	Neg.
Spinal fluid	....	....	Cl. Neg. W.
Blood sugar	....	....	80%
Blood urea nitrogen	....	....	0.015

The reports of thirty-one cases of congenitally absent gallbladder and cystic duct reveal the average age as 48 years. Thirteen patients with complete absence of all ducts and the gallbladder survived an average of seventy days. The logical deduction thus follows that the extent of congenital deficiency is in direct relation to the degree of disturbance of physiologic function.

Among congenital defects seen in man are:

1. The presence of two livers.
2. The absence of the gallbladder and all ducts or portions thereof.
3. A gallbladder and cystic ducts on the left side.
4. A bilobed gallbladder and variations in the lobulations of the liver.

Some of the lower animals which possess no gallbladder are interesting for purposes of study. These are the elephant, rhinoceros, deer, camel, horse, some rodents and a few families of birds and fish. The three forms which are available for embryologic investigation are the lamprey, pigeon and rat. No single

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etiologic factor is found to account for the absence of the gallbladder either in human beings or in lower animal species.

For absence in the human being, according to Gross,[1] there are two explanations:

1. The hepatic diverticulum arises from the foregut to form the liver, extrahepatic ducts and gallbladder. The gallbladder and cystic duct normally originate from this diverticulum as an outpocketing, but failure of the latter development would cause complete absence of the gallbladder and cystic duct.

2. The hepatic, cystic and common ducts, as well as the gallbladder, are hollow structures in early embryonic life. Later their lumens are temporarily obliterated, during the so-called solid phase through which all these structures pass. When the gallbladder bud does not resolve from its embryonic phase, there is no development of a gallbladder from the hepatic diverticulum and consequently this structure fails to develop.

Many unsatisfactory explanations are offered such as fetal peritonitis or syphilitic peritonitis in early life. It is claimed by some to be associated with harelip, cleft palate and anomalies of the ears and hands. There is no scientific proof for any of these explanations, though the prevailing opinion is that congenital defects are apt to be multiple.

Rolleston and Hayne[2] suggested unknown toxins from the mother as the causative factor of biliary congenital anomalies. They expressed the belief that nocuous metabolites are conveyed to the fetal liver, where they set up a mixed portal and biliary cirrhosis, with a descending obliterative cholangitis analogous to obliterative appendicitis. In support of their theory are several instances of parents having more than one child so affected.

Lintz[3] emphasized the presence of B bile on three occasions obtained with the Lyon-Meltzer technic in a case of absent gallbladder and ducts. The origin of this bile must have been hepatic. The common and hepatic ducts were present and no dilatation of these or of the bile canaliculi was found. One would thus assume that these did not function as storage centers

Observations During Second Admission

Date	10/14/37	10/18/37	10/20/37	10/22/37	10/25/37	10/27/37
Urine	Alb. + Bile pig.	.....	Alb. 2+ Gran. casts	.....	.....	.....
Hemoglobin	.....	85%	.....	.....	.....	.....
Red blood cells	.....	5.55	.....	.....	.....	.....
White blood cells	.....	11,700	.....	.....	.....	.....
Polymorphonuclears	.....	74%	.....	.....	.....	.....
Lymphocytes	.....	22%	.....	.....	.....	.....
Monocytes	.....	4%	.....	.....	.....	.....
Blood sugar	80%	.....	.....	.....	.....	.....
Blood urea nitrogen	0.011	.....	.....	.....	.....	.....
Cholesterol	404	.....	404	.....	.....	.....
Esters	80	.....	80	.....	.....	.....
Esters, per cent	19%	.....	17%	.....	.....	.....
Icterus index	92	90	.....	.....	125	.....
Van den Bergh	Immed.	Immed.	.....	.....	.....	.....
Phosphatase	.....	.....	.....	15.5 Un.	.....	19 Un.
Inorganic phosphates	.....	.....	.....	3.2	.....	.....

for bile. The presence of gallbladder bile in this instance throws doubt on the origin of this bile fraction. The Graham-Cole test and necropsy precluded the possibility of an intrahepatic gallbladder. His article substantiates the value of cholecystography and confirms the primary source of gallbladder bile.

The relation of the pancreas to gallbladder anomalies is infrequently mentioned in the literature. G. B. Walters feels that, clinically, absence of the gallbladder is not of particular moment except when it plays a part in the etiology of pancreatic disease. He states that Bower[4] is the only writer who gave this subject sufficient attention, as he found that the gross appearance was mentioned in only 20 per cent of the collected

Observations During Third Admission

	1937		1938				
Date	12/30	12/31	1/4	1/17	1/24	2/5	2/16
Urine	Urobil. 0 Bile + Alb. 0 Sugar 0	....	....	....	Alb. +	....	....
Hemoglobin	....	....	....	....	....	69%	....
Red blood cells	....	....	....	....	....	3.4	....
White blood cells	....	....	....	....	....	17,000	....
Polymorphonuclears	....	....	....	....	....	90%	....
Lymphocytes	....	....	....	....	....	6%	....
Blood Wassermann and Kline reactions	Neg.	....	....	....	....	....	....
Blood sugar	89%	....	....	....	....	....	....
Blood urea nitrogen	0.008	....	....	....	....	....	....
Cholesterol	.....	860	....	448	440	180	....
Esters	.....	39	....	69	78	20	....
Esters, per cent	.....	7%	....	13%	18%	11%	....
Icterus index	140	....	....	120	117	120	66
Phosphatase	....	24 Un.	....	....	....	....	....
Phosphorus	....	3.2	....	....	....	....	....
Takata-Ara test	....	....	Neg.	....	....	....	....
Lipase	....	....	1 cc. 1/20 N. Na OH	....	....	....	....
Total proteins	....	6.4	....	4.9	4.7	....	4.2
Albumin	....	4.1	....	3.1	2.7	....	2.3
Globulin	....	2.3	....	1.8	2.0	....	1.9
Ratio	....	1.8	....	1.7	1.4	....	1.2

cases. In one instance the head of the pancreas was missing; in three cases the pancreas was atrophic. In the remaining cases the organ was thickened or indurated.

In a series of 7,919 necropsies, Smith and Ball[5] found six cases of congenital absence of the gallbladder. They stressed the importance of determining its absence by means of cholecystographic studies. It has been their feeling, as well as ours, that any damage to the hepatobiliary system resulting from congenital defects may serve to augment the possibility of a fatal Heyd hepatorenal syndrome. The hemorrhagic tendencies due to vitamin K deficiency and absence of bile in the stool further diminish the probability of a favorable prognosis and warrant careful thought before surgical treatment is attempted.

Croswell[6] pointed out the importance of jaundice, white greasy stools, and enlargement of the liver and spleen associated with these congenital anomalies. He stated the opinion that the absence of the bile ducts and gallbladder exists more frequently than is recognized.

Compensatory dilatation of the bile canaliculi existed in the case here reported. Dilated bile ducts often, but not constantly, substitute as storage deposits when the gallbladder is absent. The literature fails to reveal conclusive evidence regarding this occurrence. Just what effect the back pressure of the bile would have relative to the development of cirrhosis is not known. Cirrhosis of the liver was diagnosed twenty-nine times in forty cases, in 45 per cent of the hypertrophic and in 55 per cent of the atrophic type. Unfortunately, pathologic descriptions are wanting in many of the reported cases. It is believed that our case report is the only one thus far of associated carcinoma with absence of the gallbladder and cystic duct.

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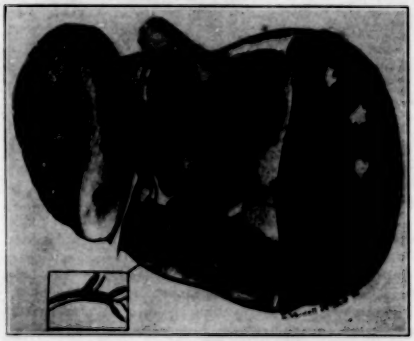
REPORT OF CASE

First Admission.—F. W., a white man aged 45, was a patient in the Philadelphia General Hospital in the service of Dr. Jump, from Sept. 5 to 14, 1937. He was wont to indulge in occasional alcoholic sprees. After imbibing too freely he was seized with vomiting of a bile stained material, with right upper abdominal pain radiating over the entire posterior part of the thorax. Vomiting continued several days after admission (until September 5). Recovery was uneventful, and physical examination revealed nothing of importance except the absence of jaundice. The only symptoms of significance in the past history were complaints of indigestion for two years, which could be attributed to heavy drinking and smoking. A questionable history of gonorrhea and syphilis fifteen years before was elicited. A diagnosis of cholecystitis and enteritis was made.

Second Admission.—The patient was in the service of Dr. L. K. Ferguson from Oct. 13 to Nov. 9, 1937. He had enjoyed good health for several days after discharge. Souring of food then commenced, with postprandial burning. The ninth day after he left the hospital, jaundice appeared with clay colored, putty-like stools and dark urine. Concurrently with the initial signs of jaundice the digestive complaints entirely disappeared. The changes noted in physical condition as compared with his



Liver: *A*, primary carcinoma of the common duct; *B*, cholangiectatic area containing sandy calculi; *C*, foci of carcinomatous suppuration.

state on the first admission were the marked icterus, drop of blood pressure from 146 systolic, 84 diastolic to 86 systolic, 54 diastolic and a diminution of pulse rate from 100 to 56, though a slow pulse is not a necessary concomitant of jaundice. A preoperative diagnosis of extrahepatic biliary obstruction with cancer of the head of the pancreas or a silent stone in the common duct was made.

The liver, which before was not palpable, now extended 2 cm. below the costal margin. A duodenal drainage showed no sign of bile after two stimulations with 40 cc. of 50 per cent magnesium sulfate solution. Dr. L. K. Ferguson performed a laparotomy and found a dense infiltration with vascular adhesions about the fossa of the gallbladder. The gallbladder and common duct could not be identified. A diagnosis was made of carcinomatous obstruction above the junction of the common and cystic ducts. It was impossible to identify any of the structures in or about the gallbladder fossa.

Third Admission.—The patient was in the service of Dr. W. E. Robertson from Dec. 28, 1937, to Jan. 10, 1938, when he was transferred to the service of Dr. J. O. Bower. He died February 23. Jaundice had been present four months; the urine was bile colored, the stools were soft and yellow to clay colored, there was marked pruritus, and weight loss had been progressive. There had been persistent morning nausea with weakness and poor appetite. Examination denoted gradual failure, with blood pressure of 90 systolic, 50 diastolic. The abdomen was tense with a questionable mass in the right upper quadrant. The size of the liver corresponded to that of the second admission. During his latter stay in the hospital he was operated on three times, in stages. On January 11, exploratory laparotomy revealed massive adhesions about the area of the gallbladder fossa. Neither the gallbladder nor the common duct could be identified. The possibility of an intrahepatic gallbladder was considered and the liver was needled. The appearance of pure bile prompted the insertion of a tube along the course of the needle. This bile drainage continued in small amounts until the patient's demise. On January 26 the liver was marsupialized. On January 31 a transhepatic cholangiostomy was performed, and on February 3 and 4 respectively mass ligatures of the muscle were necessitated by hemorrhage. Despite supportive treatment of all kinds the patient's course was progressively downward until death on February 23.

Laboratory Interpretations.—The clinical opinion was that the gallbladder was embedded in the liver. Support of this opinion was apparently furnished by the flow of bile which followed needle puncture of the liver and tube drainage.

The laboratory data on the first admission suggested an inflammatory process based on the increased total white count and the degree of granulocytosis. On the second admission this persisted, though to a smaller degree. The icterus index confirmed the evident jaundice, but the low percentage of cholesterol esters and the increase in phosphatase units indicated structural liver damage.

During the third admission, despite the marked fluctuation in cholesterol the esterified fraction remained consistently low and the phosphatase units had further increased. Total proteins fell progressively. The albumin-globulin ratio, always lower than normal, continued to fall but at no time became inverted, as is the rule in well marked cases of Laënnec's cirrhosis, although there was a definite history of alcohol addiction. The Takata-Ara test was negative, unlike that in the usual case of hepatic cirrhosis. The pressure factor, responsible for the high icterus index, was relieved by the operative procedure; hence the definite and gradual lowering of the index during the third admission.

In a case of this character, with so much structural damage, it was scarcely to be expected that vitamin K and bile or sodium cholate and vitamin K would prove of value in lessening hemorrhage. Hemorrhage was considerable, and all efforts to control it were ineffective. In the absence of further clinical exploration, the high phosphatase and low cholesterol esters were regarded as evidences of structural liver damage, probably due to carcinoma of the liver.

Pathologic Examination.—Gross Observations: Body deeply jaundiced, emaciated; kidneys, cholemic nephrosis; heart, myocardial degeneration; aorta, moderate atherosclerosis; gastrointestinal tract, mesenteric thrombosis of terminal ileum; liver and bile ducts, carcinoma, chronic inflammatory stenosis of common duct with carcinomatous obstruction; dilatation of intrahepatic bile canaliculi; multiple liver abscesses; pancreas, parenchymatous degeneration.

Histologic Observations: Heart, myocardial degeneration; lungs, chronic passive congestion, bronchopneumonia; spleen, chronic passive congestion; kidneys, cholemic nephrosis; ileum, necrosis, venous thrombosis; liver, secondary adenocarcinoma, type 3; pancreas, normal; adrenals, lipoid depletion, bile pigmentation, terminal thrombosis of central veins.

Liver: The weight was 2,500 Gm. The organ was enlarged and dark green, the upper anterior aspect of the left lobe presenting a number of yellow-gray excrescences from 5 to 10 mm. in diameter. On section they were found in the substance as well, appearing as abscesses filled with thick, reddish yellow pus. The duct radicles throughout were considerably dilated, and in the midanterior portion of the right lobe was a cavity about 4 by 4 by 8 cm. lined with red granular tissue. It communicated with the right hepatic duct just above a point of obstruction. The duct contained five sandy calculi. Elsewhere in the right lobe were several patches of firm white tumor, from 10 to 15 mm. in diameter, which appeared to encircle portal triads.

Bile Ducts: The ampulla of Vater was located in the second portion of the duodenum in about the normal position. A probe passed up the common duct encountered obstruction at the liver hilus on dissecting upward. The common duct was

found to be normal in its lower portion, but just at its bifurcation the lumen was obstructed and the duct wall merged with a nodular mass of firm white tissue with greenish yellow tinge. On section the tissue was found to fan out into liver substance over a radius of about 3 cm. No cystic duct was located.

Gallbladder: None was found, and there was no depression at its usual site.

SUMMARY

Congenital anomalies of the liver and gallbladder, although rare, are of sufficient importance to be included in a differential diagnosis of liver disease.

Ninety-six case reports are extant, and it is believed that such anomalies are more frequent than is generally supposed. A case of congenital absence of the gallbladder associated with primary carcinoma of the common duct was observed. No definite grouping of signs or symptoms can be formulated to facilitate diagnosis. This is usually made by the surgeon or pathologist.

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CANCER OF THE BREAST POSSIBLY INDUCED BY ESTROGENIC SUBSTANCE

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Estrogenic substances are now administered by physicians in a wide variety of physiologic and pathologic states. They are given to relieve menopausal symptoms, to suppress lactation, for gonorrheal vaginitis in children and for senile vaginitis and pruritus vulvae. They have been advocated for amenorrhea, abnormal uterine bleeding, dysmenorrhea, sterility, habitual abortion, chronic mastitis, painful breasts, hypertension, involutional melancholia, epilepsy, eclampsia, vomiting of pregnancy, menopausal arthritis, migraine, hemophilia, senile deafness, atrophic rhinitis and acne.

New and more potent preparations of the estrogens are being made available to the medical profession for these therapeutic uses. In addition, the public has been purchasing in drug stores and beauty shops a face cream which contains estradiol. Moore [1] has shown that this hormone is absorbed through the skin.

This widespread use of the estrogenic substances is, in the light of our knowledge of their possible carcinogenic effect, a matter for serious consideration.

It is now six years since Lacassagne's [2] important discovery that carcinoma of the breast can be induced by estrone benzoate in male mice belonging to a strain of animals the females of which frequently develop the disease. This discovery has been confirmed in several laboratories, including our own. Lacassagne,[3] Loeb [4] and others have presented evidence that the estrogens likewise induce carcinoma of the breast in female mice. It has recently been stated by Geschickter [5] that estrogens will induce carcinoma of the breast in female rats. While the data on this crucial point are not as yet adequate to prove it definitely, they are certainly suggestive.

It would have been desirable to decide this important question in the laboratory before human beings were exposed to the perils of an overdose of estrogen. These hormones have been so widely used clinically, however, that evidence as to their action on the human breast is now becoming available. The stimulus to breast growth which the estrogens exert is as evident in human beings as in laboratory animals. We have observed striking enlargement of the breasts of a number of women during the course of administration of progynon B (estradiol benzoate). MacBryde [6] has recently described this phenomenon.

Opportunities for study of the histologic features of breast growth induced in women by estrogens have been few. Our experience has been limited to four cases. In three of these the tissue available for study was adequate. In one of these cases there was only dilatation of the ducts. In both of the others there was also histologic evidence of marked stimulation of the epithelium of the breast. The gland fields were large and numerous. There were areas in which small ducts multiplied to give the picture of adenosis. There were many dilated ducts. Some formed small cysts filled with amorphous débris. Others were partly, or entirely, filled with proliferating epithelium. These changes resemble, in a general way, the histologic changes observed in the mammary glands of mice after treatment with estrogens. In mice, multiplication of the acini and dilatation of the ducts predominate. Intraductal proliferation is infrequent.

It can therefore be said that the effect of the estrogens on the mammary gland seems to be much the same in human beings as in mice. Whether or not these hormones induce carcinoma of the breast in human beings can be determined only by the careful follow-up of women given large amounts of the estrogens over a prolonged period. Allaben and Owen [7] have reported a case in which breast cancer developed following the administration of a comparatively small amount of the substance.

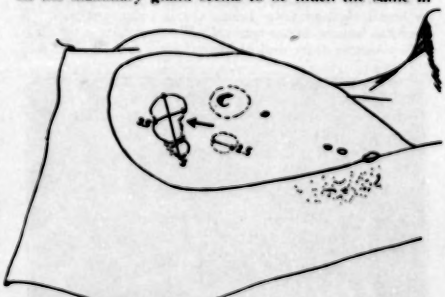

Fig. 1.—Sketch of the physical appearance in the left breast on Dec. 6, 1937. Arrow points to retraction sign.

In one of our patients carcinoma of the breast has developed. The circumstances concerning the appearance of the tumor in this patient are fully known, so

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that the case history is, we believe, of extraordinary interest and significance. We report it in detail.

REPORT OF CASE

History.—A white woman aged 47, unmarried, was admitted Dec. 7, 1937, to the Presbyterian Hospital with masses in the left breast.

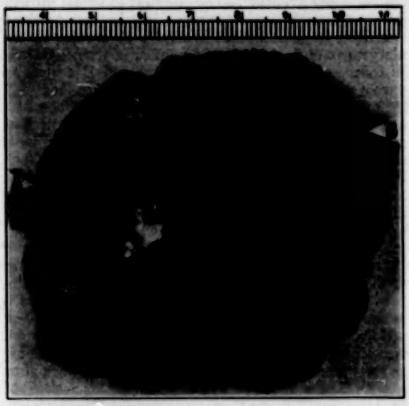

Fig. 2.—Segment of breast, including both tumors, excised for biopsy on Dec. 8, 1937. *A*, cyst; *B*, carcinoma.

Her mother had had a radical mastectomy for carcinoma of the breast eighteen years before and is living and well. A sister had had one breast removed. We do not know the diagnosis. Another sister died of tuberculosis. A third sister died

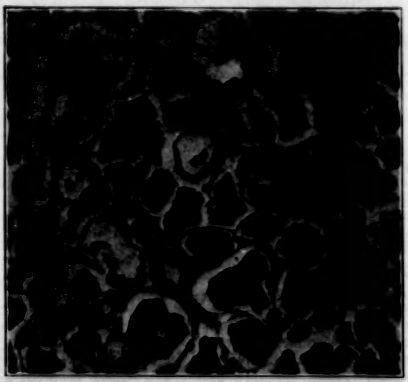

Fig. 3.—The primary carcinoma in the breast; slightly reduced from a photomicrograph with a magnification of 110 diameters.

of meningitis. A brother was killed in the war. Her father died of carcinoma of undetermined origin.

She had had various infectious diseases, none of which had any apparent relationship to the present complaint. Her menses began at 15, occurred every four weeks and lasted five or six days. They were always accompanied by headaches. During 1924 and 1925, when she was 33, she began to have metrorrhagia. Although the amount of flow was slight, she had two or three periods each month. They were accompanied by severe headaches beginning several days before each period.

In 1927 menorrhagia and metrorrhagia became so disturbing that curettage and ventral suspension were done. The uterus was large, engorged and completely retroverted. Following this operation her periods were regular and less profuse.

Her premenstrual headaches became so severe in 1929 that she was given estrogenic substance by mouth over a period of three months. The preparation used was progynon DH in the form of pills, each containing 0.0417 mg. of estradiol. The dose was one pill daily during the week preceding menstruation. It may be supposed that this therapy had little or no effect, for it is known that this preparation given by mouth in this dosage is relatively inert. The treatment did not relieve her symptoms.

In 1933, when she was 44, she was thought to have regional ileitis. She was given roentgen treatments to a 15 by 15 cm. field in the right lower quadrant. A total of 336 roentgens was given in four doses at weekly intervals during April 1935. The factors were 200 kilovolts, 50 cm. distance, 25 milliamperes, 0.5 mm. of copper and 1 mm. of aluminum filters. Following these treatments her menses ceased. She had frequent and

Fig. 4.—Dilatation of ducts to form small cysts; slightly reduced from a photomicrograph with a magnification of 10 diameters.

severe hot flashes, nausea and severe headaches. To combat these symptoms injections of progynon B (estradiol benzoate) were begun September 16. A dose of 0.33⅓ mg. in sesame oil

Estrogenic Therapy

Year	Month	Commercial Preparations of Hormone	Method of Administration	Each Dose, Mg.	Total Dose, Mg.
1929	3 months	Progynon DH	By mouth	0.042	0.875
1935 and 1936	January to April	Progynon B	24 injections	0.333	8.000
1937	January	Progynon B	7 injections	0.333	2.331
1937	February	Progynon B	2 injections	1.66	3.320
1937	February	Progynon B	6 injections	0.333	1.998
1937	March	Progynon B	3 injections	1.66	4.980
1937	April	Progynon B	5 injections	1.66	8.300
1937	May	Progynon B	3 injections	1.66	4.980
1937	June	Progynon B	6 injections	1.66	9.960
1937	July	Progynon B	8 injections	1.66	13.280
1937	August	Progynon B	2 injections	1.66	3.320
1937	September	Progynon B	7 injections	1.66	11.620
1937	October	Progynon B	3 injections	1.66	4.980
1937	November	Progynon B	5 injections	0.333	1.665
1937	December	Progynon B	1 injection	0.333	0.333
			Total dose of progynon B		79.067

was given intramuscularly each week. After the first few injections of the substance she noticed enlargement of her breasts. Her hot flashes and her nervousness were much improved. On October 22 and 23 she had a slight bloody dis-

charge, which probably represented returning menstruation. In December she had a regular period. The estrogen therapy was omitted during November and December, but in January 1936 her menopausal symptoms became so severe that it was begun again. Her symptoms then improved, and from February on her periods were regular. From Sept. 16, 1935, to April 20, 1936, she was given a total of 8 mg. of estradiol benzoate.

In April 1936 herpes zoster of the buttock and thigh developed and she entered the hospital for two weeks. At this time one of us (H. A.) examined her breasts with care and noted that they were symmetrical and did not contain any tumor masses. The mammary lobules were somewhat more readily palpable than in the average breast. There was no enlargement of the axillary lymph nodes.

In September metrorrhagia again developed, the patient having two periods of five days each of profuse bleeding. During October and November she did not menstruate at all and her menopausal symptoms returned with increased severity. She had as many as one hot flash an hour, and her headaches

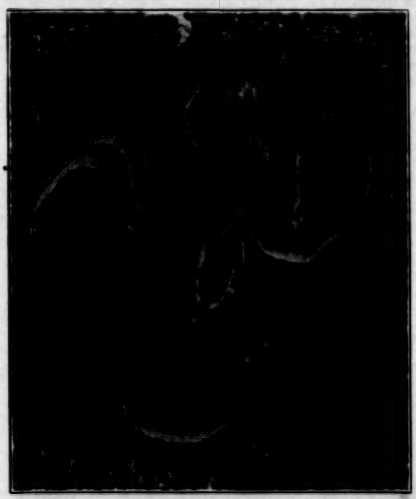

Fig. 5.—Dilated duct, filled with débris, surrounded by tumor; slightly reduced from a photomicrograph with a magnification of 10 diameters.

were frequent and severe. She had night sweats and increasing "shakiness." Neuritis developed in the neck, shoulder and arm on the right side which was so severe that in December she was admitted to the hospital for study. Again at this time her breasts were examined and no tumor masses were found.

Because of the increasing severity of the menopausal symptoms it was decided at this time by gynecologic consultants that x-ray sterilization should be done. In January 1937 she was given 600 roentgens to each of two 15 by 20 cm. pelvic fields. The factors were 200 kilovolts, 25 milliamperes, distance 50 cm., 0.5 mm. of copper and 1.25 mm. of aluminum filters.

The progynon B therapy was now begun again and was given from January to December 1937 in large doses, as shown in the accompanying table.

After each of the 1.66 mg. doses the patient complained of headache and nausea and noted swelling of her breasts. She had no period in January 1937 but had spotting on February 2 and a normal period from March 3 to 10. In April there was spotting on the 23d and 24th. In May there was a slight flow on the 20th and 21st and from the 27th to the 30th. In June she had a period which lasted from the 28th to the 30th. There was no period in July, but in August she flowed from the 4th to the 8th. In September her period again passed, but in October she flowed from the 7th to the 10th. During November and December she had no periods.

Present Illness.—About the middle of November, that is, two or three weeks before her examination on December 2, she noticed a lump in the outer lower portion of the left breast. This had not changed appreciably since she detected it.

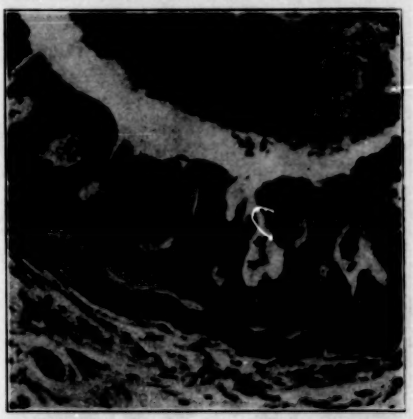

Fig. 6.—High power view of the proliferating epithelium lining the duct shown in figure 5; slightly reduced from a photomicrograph with a magnification of 180 diameters.

Physical Examination.—Both breasts were full, having definitely enlarged during the preceding year of estrogen therapy. There were palpable lobules, which were definitely thicker than before, throughout both of them. In the outer lower quadrant of the left breast, however, there were two definite and separate tumors (fig. 1). The larger measured 3.5 by 5 cm. The smaller tumor, which was slightly cephalad to the larger one, measured

Fig. 7.—Dilated ducts, partly filled with proliferating epithelium and surrounded by tumor; reduced from a photomicrograph with a magnification of 50 diameters.

2.5 cm. in diameter. The larger mass did not cast a dense shadow on transillumination, but it did cast a slight shadow. The disturbing feature was that between the two tumors there was a perfectly definite retraction sign which was elicited when the breast was moved upward and outward. This was not a "false" retraction sign; it was a "true" one. There was no

other assignable cause for it such as trauma or infection. It meant that the breast had to be considered carcinomatous until proved otherwise.

There was a large lymph node in the right axilla, and the lymph nodes in the left axilla were large and multiple. Those nearer the breast were smaller than those higher up in the axilla.

Fig. 8.—Papillary projections, without cores of connective tissue, filling a dilated duct; slightly reduced from a photomicrograph with a magnification of 120 diameters.

Operation.—On December 8 the patient was prepared for a radical mastectomy and the outer lower segment of the left breast, including the two tumors, was excised. This was a mass of mammary tissue measuring 9 by 7 by 2.5 cm. It was cut through its greatest diameter and two separate lesions were disclosed, as shown in figure 2. The larger tumor was a rounded cyst filled with thin reddish fluid and lined with smooth glistening epithelium. It measured 2.5 cm. in diameter. The smaller tumor lay at a distance of 2 cm. from the edge of the cyst. It was a stellate area of carcinoma, the cut surface of which was firm and grayish white with yellowish gray streaks and points in it. It measured 1.8 by 1 by 1 cm. A frozen section confirmed the gross diagnosis. A radical mastectomy was then done. On Dec. 29, 1939, the patient was apparently quite well.

Pathologic Examination.—Gross: The specimen consisted of the remainder of the mammary gland together with an ellipse of the overlying skin, measuring 13 by 19 cm., and the pectoral muscles and axillary contents. The breast was cut into many thin slices. The mammary tissue was more abundant and more diffuse than normal, being distributed widely throughout the perimammary fat. Scattered throughout the breast tissue were innumerable small cysts, or rather dilated ducts, which varied from 1 to 3 mm. in diameter and were filled with cloudy fluid. In the tissues surrounding the tumors excised from the outer lower quadrant of the breast there was no gross evidence of carcinoma. On the deep surface of the breast, in its middle portion, there was a firm, encapsulated tumor 1 cm. in diameter, which on section had the pinkish gray fibrous appearance of a fibro-adenoma. The nipple and the ducts beneath it were grossly normal.

The axillary contents were ribboned, and a total of nine lymph nodes, varying between 0.5 and 2 cm. in diameter, were found. The smallest of these appeared to be normal, but all the larger nodes appeared to contain metastases. Sections of many different areas in the breast were fixed in Zenker's fluid.

Microscopic: The sections through the primary tumor showed a well differentiated carcinoma, the tumor cells being everywhere arranged to form small, irregular acini (fig. 3). The individual tumor cells were of the so-called apocrine type, being small and columnar with remarkably regular nuclei and prominent acidophile cytoplasms. Mitoses were infrequent.

The mucicarmine stain failed to show any pink mucicarminophilic material in the cytoplasms of the tumor cells or in the lumens of the glands which they formed. The lumens of the glands, however, often contained concentrically ringed, calcified, hyaline concretions identical with the psammoma bodies seen, for example, in dural endothelioma or carcinoma of the ovary. These psammoma bodies were more frequent than we have ever before seen them in carcinoma of the breast.

The tumor elicited very little reaction in the nonepithelial elements of the breast. The connective tissue stroma was not much increased in density. The masses of tumor cells lay scattered loosely throughout it and infiltrated the fat in the breast. Occasional foci of lymphocytes were seen, particularly in the vicinity of dilated ducts.

The sections through the tumor area showed two other important features. The first of these was the dilatation of ducts to form small cysts lined with low cuboidal epithelium and filled with débris which sometimes contained leukocytes and foam cells (fig. 4). The second feature was the marked degree of proliferation of the lining epithelium within the ducts. The largest of these dilated ducts, like the one shown in figure 5, were lined with from two to six layers of cylindric cells thrown up into irregular, low papillary folds. Figure 6 shows this kind of proliferation under high power magnification. In smaller

Fig. 9.—Papillary projections, with cores of connective tissue, filling a dilated duct; reduced from a photomicrograph with a magnification of 100 diameters.

ducts the papillary infoldings were higher, more or less completely filling the lumens of the ducts, as shown in figure 7. Sometimes these proliferating lining cells formed long, slender papillae without any cores of connective tissue (fig. 8). In other ducts the papillae were thick and had well developed cores of connective tissue (fig. 9). Some of the ducts were more solidly filled with proliferating epithelium in an adenoid arrange-

ment, as shown in figure 10. All the cells proliferating within the ducts had the same general appearance as the cells of the carcinoma outside the ducts. They had the same rather small nuclei and prominent acidophile cytoplasms.

A section taken at a distance of 2 cm. from the edge of the carcinoma also showed small groups of carcinoma cells infiltrating the mammary fat. When these groups of carcinomatous acini lay isolated in the loose connective tissue of the breast their resemblance to normal small ducts lined by the apocrine type of epithelium was striking.

Six different blocks of tissue, taken at a distance of 3 cm. from the edge of the tumor, also showed carcinoma. Here too there were many cysts formed by dilatation of ducts.

A section through the nipple showed nothing remarkable, but sections taken through the breast tissue deep to it showed that the dilatation of ducts and intraductal proliferation, noted in the vicinity of the tumor, were equally marked in the middle of the breast. One of these sections showed a cyst which was at least 0.5 cm. in diameter. Immediately adjacent to it there was a very large duct solidly filled with proliferating epithelium (fig. 11).

A section from the lower inner quadrant of the breast showed a moderate degree of dilatation of small ducts, in some of which there was epithelial proliferation.

A section from the lateral midportion of the breast showed marked dilatation of the ducts to form the so-called apocrine

Fig. 10.—Dilated ducts solidly filled with proliferating epithelium; reduced from a photomicrograph with a magnification of 30 diameters.

cysts (fig. 12). These were lined with acidophile, columnar epithelium thrown up into low papillary folds. Other cysts of this type were scattered throughout the breast.

A section from the upper inner quadrant of the breast showed only a slight degree of dilatation of ducts and no definite proliferation of their lining epithelium.

Three blocks of tissue taken from the upper middle portion of the breast showed perhaps the most marked degree of cystic change seen anywhere in the breast. There were many widely dilated ducts lined by papillary epithelium of the apocrine type. One of these sections showed particularly well the multiplication of small ducts to give the histologic picture of what, for want of a better name, we are accustomed to call adenosis (fig. 13). This type of proliferation was seen also in other portions of the breast. Another section from this region appeared to show malignant transformation of acinar epithelium. The small, dark, cuboidal cells of the normal acini were apparently developing into larger, irregular, acidophile cells like those growing in other portions of the breast as carcinoma. We have not included an illustration of this transformation, because it is so difficult to show photographically. A section through the small, firm, encapsulated tumor lying on the deep surface of the breast showed it to be an intracanalicular fibro-adenoma.

Seven of the nine axillary lymph nodes contained metastases. In these lymph node deposits the tumor maintained the morphology of its original structure in the breast, even to the extent of forming psammoma bodies (fig. 14).

COMMENT

The features of this case that make it valuable evidence concerning the possible carcinogenic effect of estrogenic substance are the following:

1. The patient had a familial predisposition to cancer, particularly cancer of the breast. Her father died of

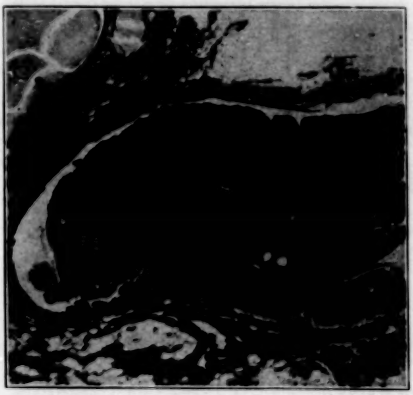

Fig. 11.—A very large duct solidly filled with proliferating epithelium; reduced from a photomicrograph with a magnification of 15 diameters.

some form of internal cancer, while her mother had had breast cancer and a sister who had lost a breast was suspected of having had cancer. We believe that both in the mouse and in man heredity plays an important part in the etiology of breast carcinoma. Its

Fig. 12.—Dilated ducts lined by the apocrine type of epithelium; slightly reduced from a photomicrograph with a magnification of 10 diameters.

familial nature in human beings is best shown by Wassink's[8] data, which are based on the family histories of 660 women with carcinoma of the breast. Two hundred and seven of these women had relatives who

8. Wassink, W. F.: Cancer et hérédité, Genetica **17**: 103-144, 1935.

had had cancer. One hundred and ninety-two of these cancerous relatives were women. One hundred and twelve, or 58.3 per cent, of these women had cancer of the breast. In the general population of Dutch women only about 10 per cent of deaths from cancer are due to breast cancer.

Fig. 13.—Multiplication of small ducts to give the picture of adenosis; reduced from a photomicrograph with a magnification of 80 diameters.

Our experimental work has shown that in mice this hereditary factor is a prerequisite for the induction of breast cancer with estrogenic substance. We have succeeded in inducing the disease only in strains of mice that have a considerable tendency to the spontaneous development of breast cancer. In a strain of mice like the C57 strain, in which the incidence of the disease is only a fraction of 1 per cent, no amount of the substance will induce breast cancer.

If this relationship between heredity and the effect of estrogen holds in human beings as well as in mice, we infer that our patient was one of those in whom estrogenic substance might have induced breast cancer, for she had a strong familial tendency to the development of the disease.

2. The patient was given estrogenic substance over a relatively prolonged period—two years and three months. It will be argued that this was too short a period for the induction of cancer. Cramer [9] has stated that if biologic time, that is, the life span, is used as a basis for reckoning, one must infer that it would take from eight to ten years of estrogenic therapy to induce cancer of the breast in a human being. He reckons one month of the life of a mouse as being comparable to about two years of life in a human being. The minimum period necessary for the induction of breast cancer in the mice that he treated was four months.

This kind of comparison has been made many times in the past in biologic work, but it seems to us a questionable one. We know, of course, that disease processes in general are more rapid in mice than they are in human beings. Our information is too inadequate, however, to permit definite conclusions as to comparative rapidity. Consider the natural history of breast carcinoma in the mouse and in man. In a large series of spontaneous mouse tumors of this type which one of us (C. D. H.) once studied, the average interval between the time that the tumor was noticed and that death occurred was six and one-half weeks. Greenwood [10] found the average duration of untreated human cancer of the breast to be 38.3 months. This might lead one to infer that the disease progresses twenty-six times as fast in mice as it does in human beings. This reasoning is probably wrong, however, because cancer is usually detected late in the mouse as compared with the human being. Moreover, mice tend to die off early with the disease as compared with human beings, because mice almost always develop multiple tumors that attain a large size and become abraded and infected.

3. Our patient received a relatively large amount of the hormone, 79.067 mg. of estradiol benzoate (progynon B). In a series of experiments carried out in our laboratory the smallest total amount of benzoate of estrone that induced breast carcinoma in a mouse was 0.45 mg. This was in a male mouse that was treated over a period of 3.5 months, beginning eleven days after birth. It is important to point out that in this experiment, as in the experiments which have been done by others, the mice have been given as much of the estrogen as they would tolerate; indeed they often died from its effects. We do not know what the minimal dose necessary to induce breast carcinoma in mice really is. It is probably considerably less than 0.45 mg. But, lacking further experimental data as to dosage, we are tempted to make a comparison of dosages on the basis of body weight between this mouse and our patient. There are, however, two reasons why we believe that it is impossible to make such a comparison. In the first place, we do not have data that afford a basis for comparing the breast-stimulating potency of benzoate of estrone with that of estradiol benzoate, weight for weight. In the second place we doubt that the effective dosages of any substances in the mouse and in man are strictly relative to body weight. All we can say

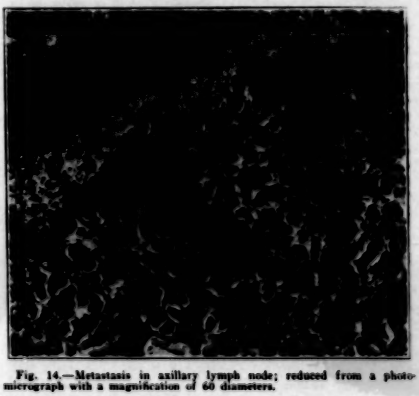

Fig. 14.—Metastasis in axillary lymph node; reduced from a photomicrograph with a magnification of 60 diameters.

about the dose of estrogenic substance in our patient is that we believe that it was sufficient to produce obvious changes in her breasts.

4. The carcinoma that did develop in our patient's left breast was of an unusual histologic type. It was

9. Cramer, W.: On the Aetiology of Cancer of the Mamma in the Mouse and in Man, Am. J. Cancer **30**: 318 (June) 1937.

10. Greenwood, Major: Report on Natural Duration of Carcinoma, Ministry of Health Report No. 33, London, His Majesty's Stationery Office, 1926.

accompanied by dilatation of ducts and epithelial proliferation throughout the whole breast, changes similar to those which we have observed in other human breasts following the administration of the estrogens.

CONCLUSION

We are not able to conclude that the estradiol benzoate (progynon B) that our patient received was certainly a contributing cause of her carcinoma, but we think it entirely possible, indeed even probable, that it was. The point can be definitely settled only by a careful and long continued follow-up of large numbers of women treated with estrogens.

Lacking this evidence at present, we are nevertheless sufficiently alarmed by our own experiences to warn against the needless and excessive administration of estrogenic substances so prevalent today. Until more is known about the effects of these substances we believe that their use should be avoided:

1. In large or prolonged doses.
2. When there is a family history of breast cancer.
3. Without initial and repeated clinical examination of both breasts.
4. In patients with chronic mastitis, carcinoma or any form of breast neoplasm, either before or after surgical or radiation treatment.

630 West One Hundred and Sixty-Eighth Street.

INDUSTRIAL DERMATITIS FROM GLOVES

EFFECT OF DERMATOPHYTOSIS (RINGWORM); "GLOVE PHYTIDS"

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A large number of workmen are required to wear leather gloves or gloves of similar type for protection while working. A definite increase in the incidence and severity of dermatophytosis has occurred during recent years.[1] This makes consideration of the subject important to dermatologists, industrial physicians and general physicians who see many cases of eczematoid dermatitis of the hands.

In this study we have endeavored to determine the relative importance of gloves and dermatophytosis of the feet (athlete's foot) in the production of a particular type of eczematoid dermatitis of the hands.

For several years we have noticed that many of the workmen in the section of our plant manufacturing tetra-ethyl lead contract eczematoid lesions of the hands. Previously the rash was considered to be an eczema having no relation to work. During these years many patients have been treated by family physicians and several have been referred in turn to dermatologists. The condition of the hands of several of these men was so bad that they could not work for many months. In some cases the condition became definitely worse as soon as the employee returned to work. In one case severe lesions of the feet and hands suggested dermatophytosis to the dermatologist. However, he felt that the lesions were not typical and that the cause was possibly idiosyncrasy to the gloves worn or to other material handled by the workman.

In March 1938 a systematic study was begun to try to determine the cause of this eczematoid dermatitis. It was found that among the 300 operators in the tetra-ethyl lead plant twenty were suffering from this particular form of dermatitis, which had been present for from a few weeks to four or five years. The men reported that there were some periods when the hands were almost free from lesions and others when the eczema was very severe. It was rather uniformly worse in summer and was better when the men were on vacation or away from the plant for week-ends.

WORKING CONDITIONS

The men all wear leather gloves which are dipped into a solution of soap chips and glycerin to make them impervious to any possible spill of tetra-ethyl lead fluid. The gloves are worn of necessity at least seven of the eight hours at work. The men wash their hands with a liquid soap having a linseed oil base. Having finished his work, each man takes a shower.

NATURE OF RASH ON HANDS

The rash first appears as small, well demarcated clusters of tiny nonimflammatory vesicles located along the sides and in the webs of the fingers and on the dorsum of the fingers and hands. Small deep seated vesicles with pearl gray centers are occasionally found in the palms. In severe cases the patches coalesce to form a continuous rash, which may extend onto the forearm. In mild cases, as some patches of vesicles clear, others form. Severe cases present all the phases of eczema with exudation, crusting, fissuring and scaling. Examples of the mild phase (case 11), mild chronic phase (case 17) and extensive acute phase (case 3) are shown in figures 1, 2 and 3.

DIFFERENTIAL DIAGNOSIS

The following conditions might produce such eczematoid lesions:

1. Dermatophytids.
2. Dermatophytosis.
3. Dermatitis due to materials coming in contact with the hands at work or at home, including such things as gloves, soaps, hair washes, powders, lotions, plants and chemicals.
4. Sensitivity to foods, medicaments and toxins. To this group we may add pompholyx, a condition which many dermatologists now feel is nonexistent.
5. Combinations of any two or more of the conditions just enumerated.

For a detailed discussion of the differential diagnosis in unselected cases, the reader is referred to the recent article by Wise and Wolf[2] and to that of White.[3]

GENERAL CONDITION OF PATIENTS

The twenty men under consideration are all in good physical condition. Recent roentgenograms of chests, complete blood counts and urinalyses gave normal results, and the blood Kahn reactions were negative. Searches for focal infection in teeth, sinuses, tonsils and occasionally in prostates were unsuccessful. There was one exception (case 6) in which the white blood count remained elevated with a normal differential count in spite of tonsillectomy, repair of the teeth and long continued prostatic massages. The condition of the feet will be discussed later.

1. White, Cleveland: The Role of Fungi in Occupational Skin Diseases, Illinois M. J. **56**: 219 (Sept.) 1929. Sulzberger, M. B., and Wise, Fred: Ringworm and Trichophytin: Newer Developments Including Practical and Theoretical Considerations, J. A. M. A. **93**: 175-179 (Nov. 19) 1929.

2. Wise, Fred, and Wolf, Jack: Dermatophytosis and Dermatophytids, with Particular Reference to Differential Diagnosis of Dyshidrosiform Eruptions of Hands and Feet, Arch. Dermat. & Syph. **34**: 1-14 (July) 1936.

3. White, C. J.: Occupational Dermatoses, Indust. Med. **6**: 135 (March) 1937.

An inquiry was made and our carefully kept records were searched in each case for possibility of an allergic background, but none was found. None of the men had ever suffered from any of the usual diseases of allergy. Possible home irritants were investigated. In some cases scratch tests were made to determine possible sensitivity to foods, danders, powders and other substances. These gave no positive results.

SKIN IRRITANTS AT WORK

The fact that in many cases the rash improved greatly or cleared entirely at home only to recur on return to work suggested a definite relation to work. The only chemical handled by the men is tetra-ethyl lead. This is handled entirely in a closed system with no contact. Absorption of tetra-ethyl lead through the skin or by inhalation produces severe systemic reactions. However, we have never had a case of dermatitis due to this fluid and we were not able to find any authentic report of a case in the literature. None of the men showed evidence of lead poisoning, though they were checked in a routine way for this at intervals of three weeks.

It was thought that the liquid soap with which the men washed their hands might be the cause of the trouble. A linseed oil base soap with very low alkalinity is used. Patch tests were made with this soap, using controls. We started at 100 per cent strength and halved the strength successively until at 1.5 per cent an occasional control was positive; at 3 per cent about one third and at 6 per cent about one half were positive. We then used these strengths (1.5, 3 and 6 per cent) for patch testing the men with active lesions and a like number with no lesions as controls. Fewer positive results were obtained with the men having the rash than with those used as controls. The men were further patch tested with linseed oil with no positive results.

At this time an employee who had been absent from work for two months because of a severe eczematoid

Fig. 1 (case 11).—Early stage of dermatitis showing groups of minute noninflammatory vesicles along sides and dorsum of fingers.

condition of the hands and forearms, as well as of the feet, returned to work in the tetra-ethyl lead buildings. His hands were completely clear but after he had worked one day, wearing leather gloves, the fine vesicular rash returned. A further two months of treatment by the family doctor at home was therefore necessary. On return to work this man was given a job mowing grass in the yard, where he was not required to wear gloves. His hands remained perfectly clear for the month in which he was so employed. He was then given gloves treated in the usual manner by dipping in a solution of soap chips and glycerin. He was told to report to us at the first sign of itchiness or rash. He reported to us the same afternoon with early lesions, which became worse and required a month at home to

Fig. 2 (case 17).—Mild chronic phase.

cure. On return to work the procedure was duplicated except that after using no gloves on outside work for a month with no trouble, he was given leather gloves which had not been treated with soap and glycerin. Again the rash quickly developed.

At this time this man, together with the nineteen other men with lesions of the hands, were patch tested with the treated and untreated leather gloves which they wear. One patch of leather was wet with the man's own perspiration, another with physiologic solution of sodium chloride. The patches were removed in twenty-four hours. The cutaneous reaction was noted and the patches were reapplied for a second twenty-four hours at the same site. The patches were placed as near to the active lesions as possible. There was not even a 1 plus reaction in the whole group.

THERAPEUTIC TESTS WITH GLOVES

Wishing to evaluate the effect of attention to the glove problem alone, we gave no treatment to the feet unless urgently needed during the first eight months of observation. The men could not work in the lead buildings without wearing leather gloves. However, during this time the hands of six of the men became so bad that they were put on work outside the buildings, where they were not required to wear gloves. In periods ranging from a few days to a month or two the eczematoid lesions of the hands cleared with no other treatment than mild lotions applied to the hands. On close inspection there were usually to be seen a few remaining noninflammatory vesicles so small that the men themselves did not notice them and considered themselves cured. However, when they resumed normal duties which required the wearing of gloves all day there was a recurrence of the lesions in each case.

The twenty men were instructed to use oversize leather gloves and to wear soft cotton gloves inside these, next to the skin. The cotton gloves are changed every other day. In every case the men reported that their hands were better, and clinical improvement ranging from little to great was noted. In not one of the cases were the hands completely cured by this means alone. The men are still following this procedure as long as there are any lesions on the hands.

There are fifty men working in the area as supervisors, clerks or laboratory workers who are not required to wear gloves. Not one of these has ever reported to the dispensary for dermatitis of the hands.

From the evidence just presented we feel that allergy to leather plays no part in our cases and probably in the great majority of similar cases. The friction, heat and excessive perspiration of the skin, with a tendency toward maceration of the horny layer, occasioned by the wearing of leather gloves is an important though not exclusive factor in the production and maintenance of these eczematoid lesions of the hands.

We next investigated the group to determine the relative importance of dermatophytosis of the feet in causing the hand lesions.

DERMATOPHYTOSIS AND DERMATOPHYTIDS

Williams [4] in 1927, studying cases of dermatophytosis involving both feet and hands, reported that, while the responsible organisms were always found by examination of scrapings from the lesions of the feet under the microscope or by cultural methods, they were seldom found in the lesions of the hands. He expressed the belief that the lesions of the hands were of an allergic nature — dermatophytids — secondary to the primary superficial lesions—dermatophytosis—of the feet. This theory is generally accepted at present, having been proved by the work of a number of investigators. The dermatophytids may appear anywhere on the glabrous skin. The primary lesions may be on the hands and the "phytids" on the feet or elsewhere, but the primary lesions are usually on the feet in the interdigits and the secondary lesions on the hands.

Our group of twenty men were examined for dermatophytosis of the feet, and clinical evidence of its presence was found in every case. The different stages or types were found. In every case white sodden plaques with vesicular or scaly lesions were found in the fourth interdigital space, frequently in the other interspaces. Hyperkeratotic patches on the balls of the feet and tense vesicles, bullae or pustules on the plantar surface, usually on the arch or inner side of the foot, were common. The sodden type with cracking and with vesiculation often seen in summer is shown in figure 4. In an occasional case there was only a little atrophy, as shown by a slightly shiny skin with a little scaling between the fourth and fifth digits.

Fig. 3 (case 3).—Extensive acute phase.

CONFIRMATORY STUDIES

Studies to confirm the clinical observations were conducted along the following lines:

1. Scrapings are taken with a sharp scalpel from active lesions of feet and hands after careful cleansing of the area with alcohol. These are soaked in 10 per cent sodium hydroxide under a cover slip ringed with Canada balsam to prevent evaporation. The slides are examined from fifteen minutes to four days later for the presence of fungi.

2. Similar scrapings from foot lesions are soaked in 80 per cent alcohol for five minutes and then planted on Sabouraud's slants. These we examined at intervals of two or three days. The pathogenic colonies of fungi usually appear in from two to four days and grow slowly, attaining a diameter of about 1 inch in from seven to ten days. The colonies have little or no color and usually have a downy appearance. Such colonies we examined in a hanging drop under the microscope for morphologic study. In doing this laboratory work we have followed the methods outlined by Weidman.[5]

Fig. 4.—Dermatophytosis. *A*, scaling and maceration between second and third toes. *B*, white sodden plaque with cracking between third and fourth toes (case 10).

3. Intracutaneous injections of commercial extracts of trichophytin and oidiomycin are made. Positive reaction indicates sensitization of the skin to these products by past or present infection with fungi or yeast. In doing these tests we used the technic of Lewis and his associates.[6] One-tenth cc. of a commercial extract of trichophytin and a like amount of oidiomycin are injected intradermally into the skin of the forearm.

An immediate wheal reaction is often present with redness, swelling and pseudopod formation. This is read ten minutes after the injection. An involved area greater than 1.5 cm. is noted as 2 plus, an area less than 1.5 cm. as 1 plus. After forty-eight hours the late inflammatory reaction is read as follows: 0 for a negative reaction, 1 plus or minus for an area of slight redness measuring approximately 0.5 cm., 1 plus for an area 0.5 to 1 cm., 2 plus for an area 1 to 1.5 cm., 3 plus for an area 1.5 to 2 cm. and 4 plus for an area 2 cm. or more.

Lewis notes that the response to dermatomycin is always positive when the subject has a dermatophytid. He further states that in cases in which the reaction to trichophytin is vigorous the prognosis is favorable.

RESULTS OF DERMATOPHYTOSIS STUDIES

A summary of results is shown in the table. The clinical diagnosis of dermatophytosis was verified in all cases that we were able to examine (eighteen) by the pathogenic fungi observed in the scrapings from the active lesions of the feet.

In cases 3, 9 and 13 we were able to obtain cultures of the fungi from scrapings planted on Sabouraud's

4. Williams, C. M.: Enlarging Conception of Dermatophytosis, Arch. Dermat. & Syph. **15**: 451 (April) 1927.

5. Weidman, Fred D.: Laboratory Aspects of Epidermophytosis, Arch. Dermat. & Syph. **18**: 415 (April) 1928.

6. Lewis, G. M.; McKee, G. M., and Hopper, M. E.: Trichophytin Test: Its Value as Diagnostic Aid, Arch. Dermat. & Syph. **38**: 713-726 (Nov.) 1938.

medium. We found the fungi in material from the hands only once, in case 12. Sensitivity to trichophytin, oidiomycin or both was demonstrated in all cases in which tests were made (sixteen) with one exception, case 2. In this case treatment had been given for two months; the toes were almost clear and the hands had been free from any lesions for three weeks.

Fig. 5 (case 20).—Fungi as seen in scrapings from toe lesion, mounted in 10 per cent sodium hydroxide; × 430. The relative size of the epithelial cells is clearly seen.

No attempt was made to identify the particular type of fungi responsible for the intertrigo except to note whether the condition was due to the commonly responsible group of fungi (Trichophyton interdigitale, Epidermophyton cruris, Trichophyton gypseum, Trichophyton rubrum) or the Oidium albicans (yeast) group. This was done for therapeutic purposes since we have found, as have others, that the yeast infections are best treated with the organic dyes. Long mycelia seldom branching are beyond question pathogenic of ringworm[7] when found in scrapings from the toes, and figure 5 demonstrates such fungi from case 20. The relative size of the fungi as compared with epithelial cells is clearly seen. Fungi from active interdigital lesions (case 13) grown on Sabouraud's medium are shown in figure 6.

COMBINED TREATMENT OF FEET AND HANDS

Prehn[7] used a powder very successfully in the treatment of a large number of men in the United States Navy. The formula which he used was salicylic acid 5 Gm., menthol 2 Gm., camphor 8 Gm., boric acid 50 Gm. and starch 35 Gm.

We have used this powder for the last twelve months with results as good as or better than we had obtained with other remedies. Each man is given two 2 ounce containers of the powder, one to use at home before coming to work and one to be kept in his locker for application after taking his shower at the end of his work period. The powder is rubbed well into, and for a distance of 1 inch around, affected areas, after first removing the tops of vesicles or bullae. Powder which does not stick to the skin is caught on a piece of paper and dusted into the bedroom slippers. In resistant cases shoes are sterilized with full strength formaldehyde. The application of the powder is so simple and clean that the men will usually cooperate. This is a big factor in chronic resistant cases. The powder used once a week is a useful prophylactic agent.

When cases were proved to be due to yeast by the finding of many budders and elongated hyphae in the scrapings, we obtained gratifying results by treating the lesions with 2 per cent gentian violet water.

Six of the patients have been actively treated for periods ranging from three to six months. Involvement was severe. Gloves were eliminated entirely when the lesions of the hands became acute and widespread. At other times soft gloves were worn under the leather gloves. Soothing lotions were used on the hands, and the feet were actively treated with the salicylic powder or with 2 per cent aqueous gentian violet. Two of the six patients have been completely cured and have remained free from any lesions for six months or longer. They are now able to wear their leather gloves with impunity. Patient 9 has had clear hands for eight months but has recently had a mild recurrence of a yeast infection of the toes which appears to be rapidly clearing with treatment. Patient 2 has had clear hands for three weeks and so has stopped treatment. He was told to resume treatment of his toes as their lesions are still mildly active, although his sensitivity to fungous products has disappeared as shown by the intracutaneous tests. The other two men have shown great improvement but still have mild lesions of the hands and feet.

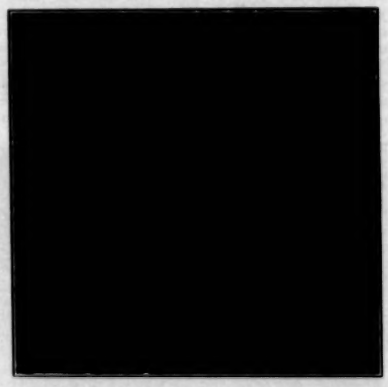

Fig. 6 (case 13).—Fungi from lesions of toe grown on Sabouraud's medium and view in hanging drop; × 950.

The dermatitis of the remaining fourteen men has been somewhat milder or more recent in origin, and we have waited until our clinical and laboratory studies were complete before starting active treatment of the feet. These have been treated for periods ranging from one week to three months. It is too early to

7. Prehn, Douglas T.: A Treatment for the Superficial Mycotic Infection of the Glabrous Skin, J. A. M. A. 111:685-688 (Aug. 20) 1938.

evaluate results in this group. Patient 18 has focal involvement of a finger nail. This is receiving roentgen treatment by a dermatologist. When it seems probable that fungi are present in the lesions of the hands, as in this case, the treatment is the same as for the feet. However, in most cases the fungi are not present in the lesions of the hands, and mild lotions are much more suitable.

DERMATOPHYTOSIS AND DERMATOPHYTIDS AMONG THE OTHER EMPLOYEES OF THE PLANT

Recently, over a period of a few days, we checked the feet of each employee coming to the plant hospital dispensary for treatments or routine examinations. No patients were included who came in with complaints referable to the feet or hands which proved to be dermatophytosis or dermatophytids. One hundred and eighteen employees were examined, and ninety-nine (84 per cent) showed clinical evidence of dermatophytosis of the toes. While only a small percentage of the plant personnel was thus examined, we feel that this gives a rough index for the plant as a whole with its 5,000 employees.

A check of our sick rolls for the year showed more time lost because of dermatophytosis than for all other skin diseases combined, infection excepted.

A close check indicates that of the 4,045 employees of this plant approximately 47 per cent wear gloves most of the time at work, while 41 per cent do not wear gloves at all. The remaining 12 per cent wear gloves less than half the time.

During the last three months we have seen forty-one patients having eczematoid lesions of the hands in which focal dermatophytosis of the feet was felt to be a factor. Of these, thirty-eight (93 per cent) wear leather gloves practically all the time at work. The rash of two of the three who did not wear gloves was probably due to a combination of mycotic and chemical sensitization. One showed definite hypersensitiveness to 0.5 per cent sodium bichromate, with which he worked. Patch tests were strongly positive, and the chemical rash on his arms cleared on removal from chemical exposure only to recur with reexposure. The dermatophytids of the hands cleared more slowly when the chemical exposure was removed, and there was a flare up of both dermatophytosis and dermatophytids on reexposure to the sodium bichromate. The other man constantly worked with torch oil, which is known to operate jointly with focal mycotic infection in producing eczematoid lesions of the hands.[8] Only one patient showed definite dermatophytids without contribution from gloves or chemical, and his condition was not chronic like the others.

With only 47 per cent of the employees wearing gloves more than half of the time, 93 per cent of the cases of eczematoid lesions of the hands secondary to dermatophytosis have occurred in this group. The frequency is seen to be fifteen times as great for those wearing leather gloves or gloves of a similar nature as it is for those not wearing gloves.

We believe that eczematoid lesions of the hands will be found with great frequency in any industrial group in which the men have a high incidence of dermatophytosis of the feet and wear leather, or gloves of a similar nature, a large part of the time.

8. Kammer, Adolph G., and Callahan, Richard H.: Torch Oil Dermatitis, J. A. M. A. **109**:1511-1516 (Aug. 20) 1938.

POLYSENSITIVITY FROM DERMATOPHYTOSIS

Since Williams[4] described the sensitizing effects of a focus of superficial mycotic infection, many studies of different phases of this subject have been made. White and Taub[9] apparently were the first to express a belief that a superficial mycotic infection could sensitize the skin to substances which otherwise were not irritating to the skin. Sulzberger and Wise[10] felt that superficial fungous infection often may be jointly responsible for chemical dermatitis or drug eruptions by a polyvalent sensitization of the skin not only to fungous products but to various chemicals and drugs.

Stokes and Kulchar[11] reported several cases in which they felt that sensitization due to dermatophytosis had increased the allergic reactivity of patients with arsphenamine dermatitis.

Beerman[12] gave an excellent review of the literature on this subject up to 1934 and cited a case of dermatitis which he felt was due to a combination of dermatophytosis and dermatophytids occurring simultaneously with and augmented by sensitization to leather.

Summary of Studies of Men with Eczematoid Lesions of Hands

Case	Fungi or Yeast in Toe Lesions	Intradermal Reaction with: Trichophytin	Intradermal Reaction with: Oidiomycin	Improvement with Soft Liner or No Gloves	Present Results
1	F	+++	++	Little	Almost cured
2	F & Y	0	0	Much	Hands clear, 3 weeks
3	F & Y	+	++	Much	Severe case, almost clear
4	F	—	++++	Little	Mild chronic case
5	F	+++	++	Moderate	Feet clearing, hands resistant
6	F	+	++++	Moderate	Feet hard to clear
7	F & Y	—	++++	Much	Hands and feet resistant, much improved
8	F & Y	++	++	Moderate	Using rubber gloves, now little improvement
9	Y	Not examined		Moderate	Hands cured, 9 months feet reinfected
10	F	++++	+++	Much	Almost clear
11	Y	—	++++	Much	Only occasional vesicle on hands
12	F	+	++	Little	Fungi found in hand scrapings, much improved
13	F	++	++	Moderate	Lost months from work, much improved
14	Not examined			Much	Completely cured, 10 months
15	F	Not examined		Much	Hands and feet clear, 3 weeks
16	F & Y	++	++++	Much	Hands clear, 6 weeks; feet almost clear
17	Not examined			Much	Completely cured, 14 months
18	Y	—	++++	Little	Infected finger nail, x-ray treatment now
19	Y	++	++++	Moderate	Have not seen for month
20	F	++	+++	Little	Feet better, hands same

Kammer and Callahan[8] reported twenty-two cases of eczematoid dermatitis of the hands, similar to our cases, which they felt were due to a combination effect from torch oil (crude kerosene) contact in sensitive men and sensitization due to superficial mycotic infection.

COMMENT

From our studies of twenty men it is our opinion that the eczematoid lesions of their hands are due to two factors: (1) leather gloves, traumatizing the skin through friction, heat and excess perspiration, and (2) dermatophytids, sensitization rash from dermatophytosis of the feet.

9. White, Cleveland, and Taub, S. J.: Sensitization Dermatoses of Nonfungous Nature, J. A. M. A. **98**:524 (Feb. 13) 1932.
10. Sulzberger, M. B., and Wise, Fred: Drug Eruptions, Arch. Dermat. & Syph. **27**:549 (April) 1933.
11. Stokes, J. H., and Kulchar, G. V.: The Infection-Allergic Complex in Arsphenamine Dermatitic Reactions, with Special Reference to Dermatophytosis, Brit. J. Dermat. **46**:134 (March) 1934.
12. Beerman, Herman: Factors Involved in Leather Dermatitis, Arch. Dermat. & Syph. **29**:671 (May) 1934.

The gloves probably make the hands more susceptible to dermatophytid formation through their macerating effects and, after their formation, tend to convert the noninflammatory dermatophytids into acute inflammatory lesions by the same mechanical processes.

For the dermatitis thus produced, we suggest the name "leather-phytids," thus expressing in two words what it requires many sentences to explain. We further suggest the term "chemical phytids" for dermatitis due to a combined sensitivity to a chemical and to superficial mycotic infection. When the chemical is known, for instance potassium bichromate, the term "potassium bichromate phytids" is appropriate.

CONCLUSION

1. We have carried out studies of an eczematoid type of industrial dermatitis of the hands appearing in workmen wearing leather gloves many hours daily. The dermatitis has been shown to be caused by two factors: (1) the traumatizing effect of the gloves, and (2) allergic sensitization of the hands due to the presence of dermatophytosis elsewhere (usually on the feet).

2. Since dermatophytosis of the feet is almost universal among industrial workers, many of whom must wear leather gloves for protection, we believe that "glove phytids" will be recognized with great frequency.

3. We have used a method of treatment which we believe is rational and which has given good results in this series of cases.

LEAD POISONING IN ROOFERS

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During the last six months eight instances of lead poisoning in roofers have been encountered at the Los Angeles County General Hospital. Since a search of the literature fails to reveal an account of such a condition in this occupational group, and since in the light of our investigations the hazard of lead poisoning is a new one in these workers, a report is considered justified.

The most important information concerning these patients is summarized in the accompanying table. All the patients are males and with but two exceptions are in early adult life. These men have been working as roofers from periods of three months to ten years. All of them give a history of holding the galvanized roofing nails in their mouths while working. None of these give a history of any other exposure to lead. The most striking facts about the entire group are found in the dates of their first attacks of colic. As long as most of these men had been working at this occupation, with but one exception none of them had had lead colic previous to May 1939. The diagnoses on admission or prior to entry are in no way surprising. Patient 1 had a diagnosis of possible lead poisoning made prior to admission on the basis of basophilic stippling in the red blood cells. Patients 5 and 6 made their own diagnoses on the basis of the previous experiences of their fellow workers. It should be noted that one of the patients had an appendectomy at the time of his first attacks of colic.

Each patient complained of colic and all but three of constipation of a moderately severe degree. Only one presented evidence of neuritis and in this instance it was limited to paresthesias involving the arm. None of the patients presented indications of notable neurologic changes. The lead line was present in but three.

In view of the conflicting reports in the literature regarding lead poisoning and hypertension[1] it is of some interest to point to the almost uniformly increased diastolic and in some instances systolic pressures observed in this group. They are certainly higher than one would expect in this age group.

Each patient had a moderate degree of anemia and basophilic stippling of the red cells, but the latter was not determined quantitatively.

The urine was examined for porphyrins in one case and none were found. As has been the practice in this hospital for the past year and a half, lead determinations were done on the whole blood rather than on the urine. All of these blood examinations were done spectrographically and in each case the amount of lead in the blood was well within the pathologically significant range. The upper limit of normal according to most of the figures available in the literature may be taken to be 0.05 mg. of lead per hundred cubic centimeters of whole blood.[2] The first patient in this group had the highest concentration of lead in the blood that we have encountered in more than 150 blood examinations. Blumberg has also reported one case in which he found a value of 1 mg. per hundred cubic centimeters of whole blood.[3]

Since all these patients are adults, x-ray examination of the long bones would not be expected to be of value.

That the roofing nails were the source of the poisoning was at once suspected. Lead is a notorious contaminant of commercial zinc, and lead poisoning has been reported in the zinc industry.[4] Samples of the nails were obtained from some of the patients and, after qualitative spectrographic analysis had indicated the presence of considerable quantities of lead, chemical analyses were made by the lead sulfate method. Approximately 3 per cent of lead was found in the galvanized coating of the nails.

The problem still remained to determine why there should be such a recent outbreak of lead poisoning in these men who had been doing the same work for periods of as long as ten years. We believe that the answer is found in the change in type of roofing nails used.

For the past ten years the various roofing concerns and lumbermen's associations have recommended the use of galvanized nails because of their weather resisting properties. In spite of these recommendations the com-

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1. Teleky, Ludwig: A Note on Blood Pressure in Lead Poisoning, J. Indust. Hyg. & Toxicol. **19**: 1-5 (Jan.) 1937. Belknap, E. L.: Clinical Studies on Lead Absorption in the Human: III. Blood Pressure Observations, ibid. **18**: 380-390 (Sept.) 1936. Gunther, G. W.: Blei und Hochdruck, Deutsche med. Wchnschr. **64**: 1146-1147 (Aug. 5) 1938.

2. Kehoe, R. A.; Thamann, Frederick, and Cholak, Jacob: Normal Absorption and Excretion of Lead, J. A. M. A. **104**: 90-93 (Jan. 12) 1935. Scott, G. H. McMillan: The Spectrographic Determination of Lead in Blood from Normal Human Subjects, Am. J. M. Sc. **195**: 622-627 (May) 1938. Willoughby, C. E., and Wilkins, E. S., Jr.: The Lead Content of Human Blood, J. Biol. Chem. **124**: 639-657 (Aug.) 1938. Wexler, I. B., and Sobel, A. E.: Spectrographic Determination of Lead in Blood Serum, Proc. Soc. Exper. Biol. & Med. **39**: 719-722 (Feb.) 1935. Blumberg and Scott.[3] Smith, Rathmell and Marcil.[4]

3. Blumberg, Harold, and Scott, T. F. McNair: The Quantitative Spectrographic Estimation of Blood Lead and Its Value in the Diagnosis of Lead Poisoning, Bull. Johns Hopkins Hosp. **60**: 276-293 (May) 1935.

4. Urtel: Bleiintoxikationen und ihre Bedeutung fur die Zinkhüttenindustrie, Ztschr. f. Gewerbehyg. **29**: 165 (Nov. 15), 184 (Dec. 15) 1932.

mon practice had been to use the so-called blued nail. These nails are easily recognized by their thin blue coating, which is due to acid treatment during manufacture. We are unable to find any appreciable quantities of lead in these nails either by spectrographic or by chemical analysis.

When the Federal Housing Administration first began to function, galvanized nails were specified, but apparently this requirement was not rigidly enforced until early in 1939. Not until this ruling was enforced did the use of these nails become general. The first of these new attacks of colic in this group of patients occurred in May 1939.

The nails now used are fourteen gage "hot-dip" galvanized nails, the size varying with the manner in which the shingles are to be laid. According to information obtained from the Columbia Steel Company, the larger sizes are most commonly coated with prime western grade zinc. Such zinc under the rejection limits set by the American Society for Testing Materials must not contain more than 1.6 per cent of lead.[5] In the smaller sizes, however, in which smoothness is essential, lead and tin up to 5 per cent of each are commonly added to the zinc in order to lower the melting point of the alloy and give a smoother coating to the finished product. There had been no recent change in the manufacture of these nails.

We have analyzed shingling nails of various sizes obtained from different manufacturers and have found a lead content of from 0.9 to 4.7 per cent in the zinc coating. These determinations were made by the dithizone method and were calculated on the ratio of lead to zinc.

As another link in this chain of evidence, we were interested in determining how much lead would be dissolved by the saliva. Approximately thirty nails having 3 per cent of lead in the coating were placed in 50 cc. of pooled saliva having a p_H of 7.0. At the end of four hours 4 micrograms of lead was found dissolved in the saliva. While at first glance this may seem like a small amount, we feel that it is significant. The daily toxic oral dose of lead has been variously estimated at from 100 to 1,000 micrograms.[6] At the rate of 4 micrograms from thirty nails it would not take so many to reach the toxic level, especially if one considers that the amounts soluble in saliva probably represent but a fraction of the amount ingested. Large amounts of zinc dust are found on the nails; some of this is probably swallowed, so that more lead is dissolved in the gastric juice.

The possibility of arsenic poisoning in these workers was recently suggested. In order to rule this out, the twenty-four hour urine from one of the patients was analyzed for arsenic and found to be normal. From 20 Gm. of nails we were able to find but 50 micrograms of arsenic.

From the stories these patients have told, we have reason to believe that we have seen only those who suffered from the more severe poisoning. Nearly all the patients can name two or three co-workers who have had similar though milder attacks.

Several of the patients were emphatic in their statements that they have always put the nails in their mouths but that they never had any trouble until the new galvanized nails were used.

In all fairness to the employers of these men, it should be stated that the workers admit that they have been told not to put the nails in their mouths. They have been told to wear "strippers" to carry the nails, but the men are equally emphatic in their statements that since they are paid by the square foot of roof finished it is impossible to shingle fast enough to make an adequate wage unless they hold the nails in their mouths. One patient reported that his daily wage dropped from $7 or $8 a day to $3.50 a day when he started to use a "stripper."

Observations in Eight Cases

Case	Age	Years Roofer	Date of 1st Colic	Date of Admission	Admission Diagnosis	Lead	Constipation	Neuritis	Colic	Lead Line	Stippling	Hemoglobin	Blood Pressure	Blood Lead Mg. per 100 Cc.
1	27	4 yrs.	8/39	9/15	Mechanical ileus? Lead poisoning	+	0	+	0	+	70%	130/90	1.0
2	28	3 yrs.	9/37	9/24	Peptic ulcer	+	0	+	0	+	.....	130/80	0.24
3	36	10 yrs.	10/39	10/14	Acute appendicitis	+	0	+	+	+	80%	132/88	0.22
4	36	1 yr.	5/39	11/15	Peptic ulcer	+	0	+	0	+	70%	128/90	0.23
5	28	1½ yrs.	12/38	12/16	Lead poisoning	0	+	+	+	+	70%	130/85	0.20
6	26	3 mos.	12/39	12/14	Lead poisoning	0	0	+	+	?	.....	140/90	0.20
7	45	6 mos.	11/39	1/ 6	Peptic ulcer	+	0	+	0	+	64%	130/80	0.12
8	44	?	9/39	10/14	Cancer of stomach	0	0	+	+	+	64%	140/80	0.34

The various authorities in the Federal Housing Administration and in the lumbermen's associations have been informed of our observations. They have brought pressure to bear on the manufacturers, who state that they will now coat the nails with an alloy of tin and zinc.

It is not our purpose in this paper to debate the diagnostic values of urine versus blood lead determinations. That is a question on which a sharp difference of opinion is expressed in the literature. We do not have the figures on the blood and the urine of these patients for comparison, yet we do feel that our work shows that the determination of the lead content in the whole blood by spectrographic means can be of definite diagnostic value. While it is true that stippling of the red cells was found in the blood of each of these patients when one considers all of the conditions in which stippling may be found, that alone cannot be taken as absolute evidence of lead poisoning. We agree with the conclusions of Blumberg and Scott that "A clinically positive blood lead (above the critical level of 0.1-0.2 mg. per 100 cc. of whole blood) has never been observed except in clinical lead poisoning or during convalescence from it; therefore, a clinically positive result indicates immediate or slightly remote lead poisoning."[3]

As has been the experience of other workers in the field, we have been unable to find any direct correlation between the level of lead in the blood and the severity of symptoms. All the patients responded promptly to calcium therapy in that their colic stopped and they were entirely symptom free. Usually the level of lead in the blood remained high and in the cases which we

5. Scott, W. W.: Standard Methods of Chemical Analysis, ed. 5, New York, D. Van Nostrand Company, 1939, p. 1071.
6. Wright, W.; Sappington, C. O., and Rantoul, E.: Lead Poisoning from Lead Piped Water Supplies, J. Indust. Hyg. & Toxicol. **10**: 234-252 (Sept.) 1928. Lanza, A. J.: Epidemiology of Lead Poisoning, J. A. M. A. **104**: 85-87 (Jan. 12) 1935.

have been able to follow for some time it remained high for a period of two or three weeks. In some instances, however, the concentration of lead in the blood has decreased dramatically following treatment. In view of the work of F. L. Smith and his co-workers at Philadelphia[7] one wonders whether serum lead determinations would be of value in the prognosis of such cases. They were able to demonstrate that while the lead content of the whole blood might remain high following lead poisoning, yet, as the symptoms subsided, lead in the serum returned to its normal value.

A FAMILIAL HEMOPOIETIC DISORDER IN ITALIAN ADOLESCENTS AND ADULTS

RESEMBLING MEDITERRANEAN DISEASE (THALASSEMIA)

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BALTIMORE

We are prompted to make this report because the cases to be described seem to represent a disorder of the blood in adolescents and adults which has hitherto received little attention. It is a chronic disturbance of erythropoiesis which is marked by microcytosis and hypochromia and by the production of red corpuscles of bizarre shape and red cells resembling targets. Normoblasts, polychromatophilic and particularly stippled red cells are found in the circulating blood. These abnormalities occur in spite of the presence of little or no anemia and even in the face of an actual increase in the red cell count above normal. The red corpuscles possess an unusually great resistance to destruction in hypotonic solutions of sodium chloride, yet there may be some evidence of increased red cell destruction in vivo. The patients may have no complaints, but splenomegaly is often found and roentgenographically demonstrable changes in the bones may be present. Our patients have all been Italians, and the disorder has been found in several generations of the two Italian families we have studied.

For reasons which will be given later, we believe that this disorder is similar to Cooley's "erythroblastic" anemia[1] or "Mediterranean disease" (thalassemia),[2] a serious and usually fatal disease of childhood. It seems probable to us that the cases we are about to describe represent a less severe form of thalassemia than is known by Cooley's name and consequently the patients have lived to adolescence and adult life. If this is true, they afford evidence supporting the view that this disorder is a hereditary anomaly of red cell formation, a possibility which has been mentioned by several students of Cooley's anemia but in favor of which there has been no evidence until recently. This would place thalassemia in the same category as familial hemolytic icterus and sickle cell anemia, two conditions with which it has much in common. The pertinent literature will be considered.

REPORT OF CASES

PATIENT M. D. and FAMILY D.—*A Sicilian youth known to have splenomegaly, hypochromic microcytic anemia and chronic low grade jaundice with urobilinuria since the age of 10; anemia "idiopathic" and failed to respond to treatment; blood marked by the presence of "target" corpuscles, bizarre poikilocytes, some erythroblasts and stippled red cells; red corpuscles showed marked resistance to destruction in hypotonic saline solution; marked erythroblastosis of the sternal marrow; increased osteoporosis and thinning of the cortex of the bones. The father, and the brother aged 30, found to have splenomegaly, icterus and the same abnormalities of the red corpuscles. Microcytosis, stippling, target corpuscles and increased resistance to hypotonic saline solution found in the blood of the mother and very slight changes in the blood of two sisters. Slight splenic enlargement in two children of one of the sisters.*

M. D., a youth aged 18, unmarried, first appeared at the Harriet Lane Home of the Johns Hopkins Hospital at the age of 10, complaining of pain in the abdomen. He was born in Baltimore in 1921 of Sicilian parents. Since the age of 2 years the skin and eyeballs had appeared yellowish, according to his mother, and on several occasions he had complained of pain in the right side of the abdomen. With these attacks, however, no increase in the yellowness of the skin or eyeballs nor any alteration in the color of the urine or stools had been noticed. There had been no illness suggestive of malaria. The patient was undernourished. There was definite jaundice of the skin and scleras. The liver was not palpable. The spleen was enlarged and its edge could be felt two finger-breadths below the costal border. Otherwise the physical examination was negative.

TABLE 1.—*Differential Counts of the Nucleated Cells in Material Obtained by Sternal Puncture from Patients M. D., V. S. and B. G.**

	Normal, Per Cent	M. D. Puncture	M. D. Biopsy	V. S.	B. G.
Leukocytes					
Myeloblasts	2.0	0.6	1.5	...	1.0
Undifferentiated myelocytes (A and B)	5.0	1.2	1.2	2.5	1.0
Differentiated myelocytes (C)					
Neutrophils	12.0	5.4	5.2	13.5	6.5
Eosinophils	1.5	1.2	...	...	...
Basophils	0.5	0.2	...	...	...
Metamyelocytes					
Neutrophils	22.0	6.8	5.4	24.0	11.0
Eosinophils	...	0.7	0.8	0.5	...
Polymorphonuclears					
Neutrophils	23.0	6.0	5.0	20.0	36.5
Eosinophils	2.0	1.2	0.4	1.0	3.0
Basophils	0.2	...	...	...	...
Lymphocytes	30.0	4.5	4.8	9.0	36.5
Plasma cells	0.4	0.2	...	...	...
Monocytes	2.0	0.5	...	1.0	1.5
Reticulum cells and macrophages	0.2	...	...	...	...
Mitotic figures	...	0.4	0.8	...	...
Unclassified cells	...	0.2	...	...	...
Megakaryocytes	0.4	...	...	...	...
Erythrocytes					
Primitive erythroblasts	...	2.5	1.2	...	...
Macroblasts	4.0	8.5	4.8	2.0	2.0
Normoblasts	18.0	61.5	66.0	27.0	7.0

* In the case of M. D. smears were also made of marrow obtained at biopsy, and the differential count on these is also given.

Laboratory examination revealed erythrocytes 4.28 million per cubic millimeter content, hemoglobin 7.5 Gm., volume of packed red cells 27.5 cc., mean corpuscular volume 65 cubic microns, mean corpuscular hemoglobin 18 micromicrograms and mean corpuscular hemoglobin concentration 27 per cent. The icterus index varied from 13 to 28. The serum bilirubin (van den Bergh) was 4 mg. per hundred cubic centimeters. The

7. Smith, F. L. 2d; Rathmell, T. K., and Marcil, G. E.: The Early Diagnosis of Acute and Latent Plumbism, Am. J. Clin. Path. **B:** 471-509 (Sept.) 1938.

Dr. Murray Fisher and Miss Regina Weistock brought two of these cases to our attention.

From the Department of Medicine, the Johns Hopkins University School of Medicine, and the Medical Clinic, the Johns Hopkins Hospital.

1. Cooley, T. B.; Witwer, E. K., and Lee, Pearl: Anemia in Children with Splenomegaly and Peculiar Changes in Bones: Report of Cases, Am. J. Dis. Child. **34:** 347-363 (Sept.) 1927.

2. Whipple, G. H., and Bradford, W. L.: Racial or Familial Anemia of Children Associated with Fundamental Disturbances of Bone and Pigment Metabolism (Cooley-von Jaksch), Am. J. Dis. Child. **44:** 336-365 (Aug.) 1932.

fragility test on two occasions showed a slightly increased resistance of the erythrocytes, hemolysis beginning in 0.42 per cent saline solution and being complete in 0.28 per cent. In a specimen of normal blood hemolysis commenced at 0.42 per cent and was complete at 0.32 per cent. The reticulocyte count was 6.6 per cent. The stained smear showed marked anisocytosis, poikilocytosis and hypochromia of the erythrocytes as well as a moderate number of stippled cells, but no nucleated red cells were observed. The total and differential leukocyte counts, the platelets, bleeding time, clotting time and clot retraction were all normal. No sickling could be demonstrated. The blood Wassermann reaction was negative. The urine was negative for bile but positive for urobilin. Roentgenograms of the head and long bones were considered normal. The jaundice and the blood picture were the subject of much speculation, but no diagnosis was made. The patient was observed for one year. No significant change in the degree of jaundice or in the results of blood examination was noted.

Fig. 1.—Patient M. D.

He next appeared at the age of 17, in December 1938, when he was admitted to the medical service with mild bronchopneumonia, from which he recovered quickly. The interval history revealed good general health. He had been working as a barber. In addition to the signs of pneumonia, the physical examination revealed definite although slight icterus of the skin and scleras, slight exophthalmos and a spleen which was readily palpable 3 cm. below the costal border. The edge was rounded and the entire organ seemed somewhat nearer the midline than usual. The liver was not enlarged, the cranium seemed normal in shape (fig. 1) and there was no pallor.

On laboratory examination, as had been noted seven years before, the red corpuscules were small and poorly filled with hemoglobin (table 2). Their mean diameter in wet films was 7.03 microns and the mean corpuscular thickness 1.68 microns. In the stained smear (fig. 2) there was considerable anisocytosis, poikilocytosis and hypochromia, as well as many cells with an outer rim of hemoglobin-containing material and a central area of the same density separated by an intervening ring of lighter staining material to which the name "target corpuscles" has been applied.[3] There were numerous stippled cells, but nucleated red blood cells were found only after the injection of epinephrine (from 4 to 6 per 200 leukocytes).

In wet films of blood numerous poikilocytes of very bizarre forms were present. These included narrow irregular bands, curled and twisted in various shapes and forming the letters T and I, as well as pear-shaped and elliptic forms. Similar preparations made from the blood of a patient with hypochromic microcytic anemia of the type resulting from iron deficiency[4] failed to show these bizarre forms of red corpuscles. It is noteworthy that long, filamentous processes extending out from the red corpuscles and the oat-shaped and sickled forms characteristic of sickle cell anemia were not found.

No malaria or other parasites were observed in wet or stained films of blood, in thick drops or in blood obtained after the injection of epinephrine and concentrated.

The unusual reaction of the red corpuscles to hypotonic solutions of sodium chloride attracted our attention. Although hemolysis commenced in 0.48 or 0.45 per cent saline solutions as it did in specimens of normal blood, an increase in the degree of hemolysis did not take place quickly as it normally does (fig. 3). In the specimens of normal blood hemolysis was well marked in 0.42 per cent saline solution, whereas in the patient's blood the increase in the degree of red cell destruction in tubes containing more dilute saline solutions was very gradual, and well marked hemolysis first occurred in 0.30 per cent salt solution. The increased resistance of many of the red corpuscules to the action of hypotonic solutions was further indicated by the fact that, whereas complete hemolysis with no remaining residue of red cells took place in from 0.36 to 0.30 per cent saline solutions in the case of normal blood, a residue of cellular material persisted sometimes even in tubes containing 0.03 per cent sodium chloride. The concentration of salt solution necessary to produce complete hemolysis varied on different occasions between 0.18 and 0 per cent. The pale gelatinous scum remaining in the hypotonic solution of salt was examined microscopically and found to consist of "shadows" of red corpuscles.

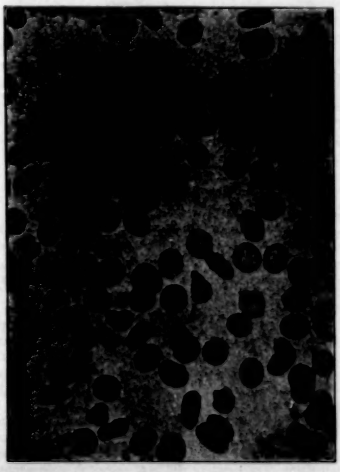

Fig. 2.—Stained smear of blood of patient M. D., showing the marked hypochromia, poikilocytosis and microcytosis as well as a few target cells. Oil immersion, × 800.

A fragility test carried out on the blood of a patient whose red cells, as the result of iron deficiency, were as small and hypochromic as those of this patient gave the following results: beginning hemolysis at 0.48 per cent, well marked hemolysis at 0.42 per cent, complete hemolysis at 0.30 per cent.

3. Barrett, A. M.: Special Form of Erythrocyte Possessing Increased Resistance to Hypotonic Saline, J. Path. & Bact. 46: 603-618 (May) 1938.

4. Wintrobe, M. M., and Beebe, R. T.: Idiopathic Hypochromic Anemia, Medicine 19: 187-243 (May) 1933.

Washing the red corpuscles several times in physiologic solution of sodium chloride did not alter their resistance to hypotonic solutions (beginning hemolysis at 0.48 per cent, well marked hemolysis at 0.24 per cent, complete hemolysis at 0.18 per cent; corresponding values for normal blood: 0.48, 0.39 and 0.30 per cent). Dilutions of the blood also were made in erythrocyte counting pipets, the diluting fluids being various strengths of salt solution. In a typical experiment, 30 per cent hemolysis was found in 0.48 per cent sodium chloride solution, 63 per cent in 0.30 per cent and 100 per cent in 0.18 per cent.

The icterus index ranged from 10 to 35. The serum bilirubin (van den Bergh) was 1.8 to 2.2 mg. per hundred cubic centimeters, indirect. No hemolysins could be demonstrated by the Donath-Landsteiner test for autohemolysins.

After the subsidence of the pneumonia, the leukocyte count was 8,500 per cubic millimeter. The differential count was as follows: juvenile neutrophils 3 per cent, segmented neutrophils 47 per cent, eosinophils 8 per cent, basophils 1 per cent, lymphocytes 34 per cent, monocytes 7 per cent. Platelets were normal in number and the bleeding and coagulation times were normal.

The sternal bone marrow was obtained by puncture and by biopsy (figs. 4 and 5). The results were the same by the two methods, and the details are given in table 1. The essential feature was a striking increase in nucleated red blood cells, especially normoblasts. Younger cells were present, but even the least mature erythroblasts did not have the appearance of the megaloblasts of pernicious anemia. There was, in addition, a slight increase in eosinophils. It is noteworthy that, in spite of the erythroblastosis of the marrow, no normoblasts were found in the circulating blood except after the injection of epinephrine.

The urine gave a negative test for bile, and sometimes a negative and at other times a faintly positive reaction for urobilin. The test for urobilinogen in fresh urine was positive in a dilution of 1 to 20 (control 1 to 5). The stool was repeatedly negative grossly and by guaiac test for blood, as well as microscopically. Roentgenographic examinations of the gastrointestinal tract for a possible source of chronic blood loss were negative. Analysis of fasting gastric contents revealed values of 8 for free and 22 for total acid. The basal metabolic rate was + 2. The bromsulphalein test of liver function using 5 mg. per kilogram showed 5 per cent retention in one half hour, a normal value. A skin test with an extract of the fava bean was negative. The serologic test for syphilis (Eagle) was negative.

Roentgenograms were interpreted as follows: The long bones showed evidence of increased osteoporosis and thinning of the cortex, particularly the femurs (fig. 6). The skull was normal.

Although the blood showed the hypochromia and microcytosis typical of iron deficiency, there was no response to ferrous sulfate 1.2 Gm. daily by mouth for twelve days (fig. 7) or to the same daily dose of iron plus 0.38 Gm. of copper sulfate (in divided doses) over a thirteen day period. Daily reticulocyte counts revealed an irregular fluctuation between 1 and 5 per cent. On the ninth day of treatment with iron and copper, the reticulocytes increased to 7.2 per cent. At this time there were a slight fall in the red cell values and a rise in the serum bilirubin level.

Examination of the blood one month after discharge from the hospital revealed no significant change.

C. D., the father of M. D., aged 57, was born in Sicily. He had had jaundice and a large abdomen throughout childhood. He was said to have been born with malaria and to have had it until the age of 20. He had had no chills in the past twenty years. A "tumor" in the abdomen had been noted on several occasions, and in 1932, when he came to this hospital because of pain in the epigastrium, examination revealed that he had an enlarged spleen. On examination of the blood it was found that the erythrocyte count was somewhat high (6.20 million) and there were microcytosis and hypochromia (mean corpuscular volume 72 cubic microns, mean corpuscular hemoglobin 17 micromicrograms, mean corpuscular hemoglobin concentration

TABLE 2.—*Summary of Clinical and Laboratory Data of Fourteen Persons Examined* *

Family	Doe.								S.	Gab.				
	F	M	Children				Grandchildren			F	M	Children		
Patient	CD	JD	PD	MD	RD	ADB	FB	CB	VS	BG	SG	VGC	AG	EG
Sex	♂	♀	♂	♂	♀	♀	♂	♂	♂	♂	♀	♀	♀	♂
Age	57	55	30	17	13	27	8	7	60	54	51	25	21	19
History														
Malaria	+	±	0	0	0	0	0	0	0	0	0	0	0	0
Jaundice	+	+	0	+	0	0	0	0	0	0	0	0	0	0
Physical examination														
Jaundice	0	0	0	+	0	0	0	0	+	±	0	0	0	0
Splenomegaly	+	0	+	+	0	0	+	±	+	0	0	0	0	0
Urobilinuria	+	..	+	+	..	0	0	0	+	+	..	..	..	..
Blood group	B	A	B	0	0	B	B	A	0	0	0	0	A	0
Blood examination														
Erythrocytes in millions, cu. mm.	5.6	6.3	6.2	6.2	5.4	5.4	5.2	5.0	6.3	5.5	4.5	5.2	4.1	5.7
Hemoglobin, Gm. per 100 cc. of blood	10.8	12.6	12.0	10.1	13.0	12.5	13.2	14.0	13.6	12.1	14.0	12.0	12.0	12.9
Volume of packed red cells, cc. per 100 cc. of blood	37	38	41	36	38	41	41	39	42	41	43	42	36	45
Mean corpuscular volume, cubic microns	67	61	66	57	70	75	79	77	67	75	96	81	94	79
Mean corpuscular hemoglobin, micromicrograms	20	20	20	16	24	24	26	28	22	22	31	23	30	22
Mean corpuscular hemoglobin concentration, per cent	29	33	30	28	34	31	32	36	33	29	32	29	32	29
Icteric index of plasma	10	8	12	10-35	4	4	4	4	9-15	12	10	10	11	11
Van den Bergh test	tr.	tr.	tr.	ind. 1.1-2.2	0	0	0	0	ind. 0.9	ind. 0.9	tr.	tr.	tr.	tr.
Reticulocytes, per cent	4.2	2.3	1.8	3.6	0.8	1.2	0.4	0.2	1.4	1.6	0.6	1.6	0.2	0.4
Abnormal erythrocytes														
Hypochromia	++	+++	++	++	+	0	+	0	++	+++	0	++	0	++
Anisocytosis	++	++	++	++	0	0	0	0	++	++	++	++	0	++
Poikilocytosis	++	+	++	++	0	0	0	0	+	+	0	++	0	+
Target cells, average number per oil immersion field	2	4	12	8	0	0	0	0	4	6	0	8	0	2
Polychromatophilia	+	+	+	0	0	0	0	0	0	0	0	+	0	0
Stippling, average number per 40 oil immersion fields	5	2	0	29	0	0	0	0	10	19	4	12	3	12
Nucleated red cells, number per 200 leukocytes	0	0	1	64	0	0	0	0	0	0	0	0	0	0
Spherocytes	oc.	oc.	rs.	rs.	rs.	0	0	0	0	0	oc.	rs.	rs.	rs.
Fragility test														
Hemolysis begins	0.45	0.45	0.48	0.48	0.48	0.45	0.45	0.42	0.45	0.42	0.48	0.42	0.48	0.45
Hemolysis well marked	0.30	0.36	0.36	0.33	0.45	0.42	0.42	0.36	0.30	0.30	0.45	0.30	0.42	0.36
Hemolysis complete	0.21	0.24	0.02	0.03	0.33	0.33	0.33	0.30	0.21	0.21	0.33	0.03	0.32	0.21

* In this table and in the case reports, the following abbreviations are used: + indicates present, ++ moderate, +++ marked, ± doubtful, 0 absent, rs. rare, oc. occasional, tr. trace, ind. indirect reaction.

† In this case there were found 4 to 8 nucleated red cells per 200 leukocytes following the injection of epinephrine.

In every subject normal values were obtained for the total and differential leukocyte counts and for the platelet counts, and the serologic test for syphilis (Eagle) was negative.

25 per cent). Concentration of dye by the gallbladder was poor. Nevertheless, his general health had been satisfactory enough for him to be able to do hard labor. He returned in 1939 at our request, when examination revealed no definite jaundice; the liver was not palpable but the spleen could be felt easily, descending 3 cm. below the left costal border. Laboratory studies (table 2) revealed a normal erythrocyte count with

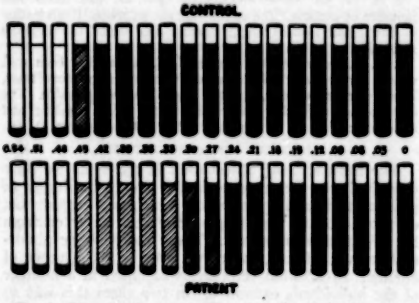

Fig. 3.—Diagrammatic representation of results of fragility test of blood of patient M. D. and of normal blood. The clear tubes indicate no hemolysis, light hatching indicates slight hemolysis, heavy hatching marked hemolysis. Note the early appearance of well marked hemolysis and the disappearance of all cell residue in the sample of normal blood, and the slow development of hemolysis and persistence of corpuscular residue in the patient's blood.

microcytosis, hypochromia, stippled cells, target cells and numerous poikilocytes. There was, in addition, increased resistance of the erythrocytes to hypotonic saline solution, as well as slightly elevated serum bilirubin and urobilinuria.

J. D., the mother of M. D., aged 55, was likewise born in Sicily. She was not known to be related to her husband before marriage, but their families had resided in the same village for several generations and therefore relationship could not be excluded with certainty. There was an uncertain history of malaria in childhood. In 1930 she was found to be jaundiced and operation revealed cholecystitis and cholelithiasis. The spleen has never been palpable. Laboratory studies showed a high erythrocyte count; microcytosis, hypochromia, stippling, poikilocytes of bizarre shape and target corpuscles, slightly increased resistance of the erythrocytes to hypotonic saline solution and normal serum bilirubin (table 2).

CHILDREN of C. D. and J. D.—1. A boy, Sicily, died at 7 months of "malaria."

2. A girl, Sicily, died at 6 months of "malaria."

3. P. D., a man aged 30, born in Sicily, had always been well, with no history of malaria or jaundice. He had a marked funnel breast. The liver was at the costal border. The spleen was easily palpable 1 cm. below the costal margin. There were a high normal erythrocyte count, microcytosis and hypochromia, occasional spherocytes as well as bizarre poikilocytes, target cells, occasional normoblasts, increased resistance of the erythrocytes to hypotonic saline solution and slightly increased serum bilirubin as well as urobilinuria (table 2).

4. A. D. B., a woman aged 27, born in Sicily, had never been ill. The spleen was not palpable and results of laboratory studies were negative except for slight microcytosis and hypochromia (table 2). She was married and had three children.

4a. F. B., a boy aged 8, had a definitely palpable spleen but results of other studies were essentially negative (table 2).

4b. C. B., a boy aged 7, had a questionably palpable spleen. Results of other studies were negative (table 2).

4c. J. B., a boy aged 19 months, was not examined.

5. M. D., a boy aged 17, was our first patient.

6. R. D., a girl now aged 13, had always been well. Microcytosis and hypochromia of the erythrocytes were the only abnormal features (table 2).

The occurrence in several members of this Sicilian family of splenomegaly, microcytosis, hypochromia and increased resistance of the erythrocytes brought to mind two Italian patients with somewhat similar abnormalities who had been examined two years before. They were asked to return and additional studies were obtained on both, as well as on the entire family of one of them (table 2):

PATIENT V. S.—*A Neapolitan found to have splenomegaly, microcytosis, hypochromia, target corpuscles, marked stippling of the red cells and increased resistance of the corpuscles to hypotonic saline solutions.*

V. S., a man aged 40, born in Naples, stated that he had not had malaria, jaundice or swelling of the abdomen. He had three children, two by his first wife, who was Italian, and the third by his second wife, who was Irish. The last child was said to be well but nothing is known about the first two. None were available for study. This patient had been observed in the dispensary of the Johns Hopkins Hospital for several years because of dizzy spells and tinnitus, associated with fear. His personal misfortunes give adequate justification for the latter. On examination in 1936 the spleen was discovered to be palpable 3 cm. below the costal margin; a somewhat high erythrocyte count (6.44 million), microcytosis, hypochromia, marked stippling of the red corpuscles, increased resistance of the cells to hypotonic saline solutions and an icterus index of 20 were found. Analysis of the blood and urine for lead yielded normal values (0.05 mg. per hundred grams of blood, 0.07 mg. per twenty-four hour specimen of urine) and there was nothing in the history or physical examination to suggest lead poisoning. Furthermore, an attempt to mobilize lead from the bones by giving ammonium chloride was unsuccessful. The bromsulphalein test of liver function showed 15 per cent retention.

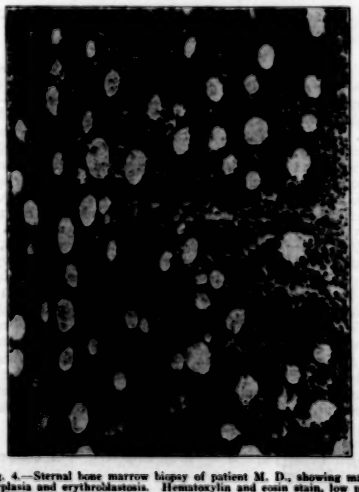

Fig. 4.—Sternal bone marrow biopsy of patient M. D., showing marked hyperplasia and erythroblastosis. Hematoxylin and eosin stain, low power magnification, × 125.

Reexamination in 1939 revealed a man of short stature and large head with a rather high forehead and narrow palpebral orifices with drooping outer corners (fig. 8). The spleen was easily felt 4 cm. below the left costal border. The laboratory studies, like those three years before, showed microcytosis, hypochromia, increased resistance of the erythrocytes to hypotonic saline solution, elevated serum bilirubin with urobilinuria and a striking degree of basophilic stippling of the erythrocytes (table 2). Roentgenograms of the skull and long bones showed

no abnormalities. Sternal marrow puncture revealed a slightly greater proportion of normoblasts than is normal (table 1). Treatment with ferrous sulfate 1.2 Gm. daily was without effect on the blood.

PATIENT B. G. and FAMILY G.—*An Italian found to have slight anemia, microcytosis, hypochromia, target corpuscles, very marked stippling, increased resistance of red corpuscles to hypotonic saline solutions and slight icterus. Similar observations on one daughter, and less marked changes in the blood of one son. Mother's blood found to be somewhat macrocytic. Slight macrocytosis in the blood of one daughter.*

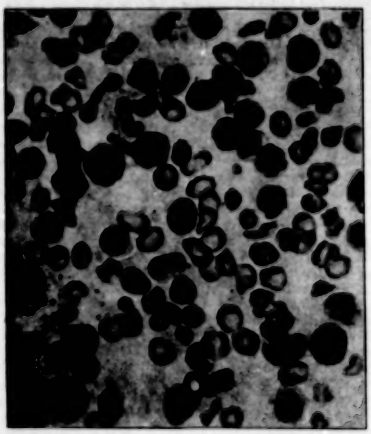

Fig. 5.—Smear of material obtained from patient M. D. at sternal bone marrow biopsy, showing numerous nucleated red cells. Wright's stain, oil immersion, × 800.

B. G., a man aged 54, married, was born in a hilly part of central Italy, where, according to the patient, malaria is unknown and no children have been noted to have jaundice, large heads or large abdomens. He married a woman from the same locality and came to America thirty-four years ago. He never had malaria or jaundice to his knowledge and had never been exposed significantly to lead. He had numbness and tingling of the fingers in cold weather for several years, and acrocyanosis had been noted on examination. It was this symptom which brought him to the hospital. In general his health had been good. Laboratory studies showed hypochromia and microcytosis, numerous target cells (fig. 9), increased resistance of the erythrocytes to hypotonic saline solution, elevated serum bilirubin with urobilinuria, and marked basophilic stippling of the erythrocytes as well as occasional normoblasts. Analysis of the blood for lead gave a normal value (0.05 mg. per hundred grams). The bromsulphalein retention was 7 per cent and the plasma uric acid was 4.4 mg. per hundred cubic centimeters. Reexamination (table 2) confirmed the data just noted. The scleras were slightly icteric. At times the spleen has been thought to be palpable by some observers. The cranium is normal in shape.

S. G., aged 51, wife of B. G., was born in the same part of central Italy as was her husband. She had never had malaria or jaundice and recalls no jaundice in any member of the family. She had had one attack of pain in the right upper abdominal quadrant, but the roentgenographic appearance of the gallbladder and gastrointestinal tract was normal. The liver and spleen were never palpable and no jaundice was noted on many examinations. Examination of the blood revealed moderate macrocytosis and occasional spherocytes (table 2).

CHILDREN of B. G. and S. G. (all born in America).—1. V. G. C., a woman aged 25, married, stated that at the age of 14 acrocyanosis was noted in the fingers; at 22 she was found to have an apical pulmonary lesion, considered to be tuberculous, which is now arrested. There was no history of malaria or jaundice. The spleen was never palpable. Laboratory studies showed hypochromia of the erythrocytes, target cells, stippling and greatly increased resistance to hypotonic saline solution (table 2).

2. A. G., an unmarried woman aged 21, had never had jaundice or malaria. The spleen was not palpable. Examination of the blood showed slight anemia and slight macrocytosis (table 2).

3. E. G., an unmarried man aged 19, had always been well except for frequent infections of the upper respiratory tract. There was no jaundice, and the spleen was not palpable. The erythrocytes showed hypochromia, target cells, stippling and increased resistance to hypotonic saline solution (table 2).

SUMMARY OF OBSERVATIONS

The most striking observation in the cases we have described was the presence in the blood of a degree of poikilocytosis and hypochromia which was entirely out of proportion to what might have been expected from the slight anemia present. These morphologic abnormalities were found, moreover, even in the absence of anemia. In addition, stippling was noted in a number of the individuals examined. In two cases this was so marked that poisoning with a heavy metal was suspected. Other signs of disturbed erythropoiesis were usually lacking, although slight polychromatophilia was observed in a few instances and an occasional normoblast was found in the blood of two individuals (P. D. and B. G.). It should be mentioned, however, that pronounced erythroblastosis was observed in the sternal bone marrow of another patient (M. D.) in whose blood no normoblasts were found except after the injection of epinephrine. Slight osteoporosis was demonstrated roentgenologically in this case.

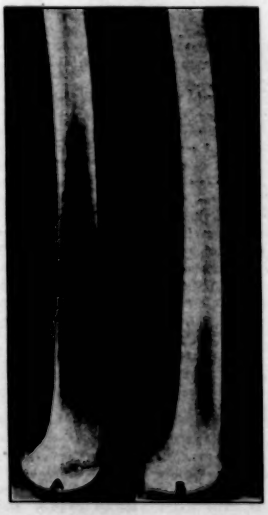

Fig. 6.—Femur of patient M. D. (*A*) compared with that of a healthy boy of the same age (*B*). Note the thinness of the cortex and the general decreased density.

The poikilocytosis was even more striking in wet films of blood than in fixed preparations, and very bizarre forms such as those described in Cooley's anemia were numerous in some instances. In the stained films an unusual type of poikilocyte was frequently seen which, because of the presence of a hemoglobin-containing circle in the center of a pale ring-like corpuscle, has been called a target cell.[5] The cells have been recently studied by Barrett[3] and others,[5] whose observations will be described shortly.

5. Haden, R. L., and Evans, F. D.: Sickle Cell Anemia in White Race: Improvement in Two Cases Following Splenectomy, Arch. Int. Med. 60: 133-142 (July) 1937.

A marked degree of resistance of the red corpuscles to the hemolyzing effects of hypotonic saline solutions attracted our attention at once. This resistance was so great that in several instances a pale, somewhat gelatinous layer remained even in tubes containing distilled water. The decreased fragility of the cells was also

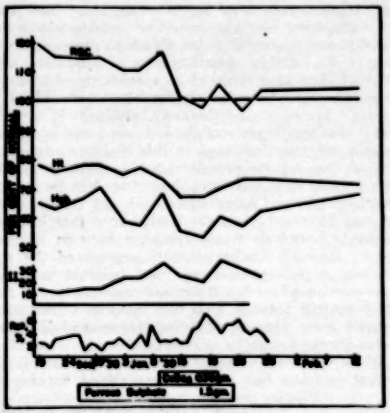

Fig. 7.—Blood data of patient M. D., showing the ineffectiveness of treatment with iron and copper. The red cell count (R. B. C.), hemoglobin (Hgb.) and volume of packed red cells (Ht.) are presented in proportion to the average values in the normal male. Note that the red cell count was normal or above normal whereas the hemoglobin and volume of packed red cells were below normal, the former being proportionately lower than the latter. These differences were evident in the low values obtained for mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration. Icterus index and reticulocytes are recorded in absolute terms, the former in units (normal 3 to 7), the latter in percentage. The figure for copper sulfate represents the total dose, whereas that for ferrous sulfate is the daily dose.

indicated by the fact that the supernatant fluid in tubes containing red corpuscles in hypotonic solutions did not become a deep red (well marked hemolysis) until solutions of 0.36 to 0.30 per cent were used (fig. 3), whereas in normal blood hemolysis is usually well marked in a 0.42 per cent solution. That the increased resistance of the corpuscles could not be attributed solely to their small size was suggested by the fact that the fragility of the corpuscles of a patient with hypochromic microcytic anemia of the iron deficiency type was quite normal.

Although the volume of packed red cells and particularly the hemoglobin content of the blood were moderately or slightly reduced below normal in seven instances, the red cell counts were normal or even unusually high (fig. 10). The red cell count of our first patient was 6.43 million when the hemoglobin was 10.3 Gm. and the volume of packed red cells 36.7 cc. This erythrocytosis is of interest because, in cases of hypochromic microcytic anemia due to iron deficiency, after effective treatment the increase in the red cell count may be so rapid that it may be well above normal when the hemoglobin and volume of packed red cells are still low and microcytosis and hypochromia are still present.[4] The high red cell counts found in our cases may represent an attempt on the part of the bone marrow to compensate for the formation of faulty red corpuscles by producing many of them.

In addition to the abnormalities of the blood, in five instances splenomegaly, slight icterus and urobilinuria were found. It may also be noted that in spite of thorough study of our three original patients (M. D., V. S., B. G.), no etiologic agent was discovered and, in the two instances in which it was attempted, iron therapy failed to alter the microcytosis or hypochromia.

All of the abnormalities mentioned, namely poikilocytosis, target cells, hypochromia, stippling, increased corpuscular resistance, splenomegaly and bilirubinemia or urobilinuria, were found in four of the persons examined (C. D., P. D., M. D., V. S.); in four more (J. D., B. G., V. G. C. and E. G.) only splenomegaly was lacking; in two children (F. B. and C. B.) there was slight splenic enlargement without significant changes in the blood; of the remaining four persons, all females, there was microcytosis without other significant changes in two (R. D. and A. D. B.) and slight macrocytosis as well as stippling in two (S. G. and A. G.). Thus none of the fourteen persons studied lacked some suggestion of hemopoietic disorder and in eight the abnormalities were well marked (fig. 10). It should be emphasized that in none of these individuals were there complaints referable to the blood disorder. Three generations were studied in one family and two in another. All of the subjects of this report were Italians.

RELATION TO OTHER BLOOD DISORDERS

The condition we have described brings to mind three well recognized familial disorders of the blood, namely familial hemolytic icterus, sickle cell anemia

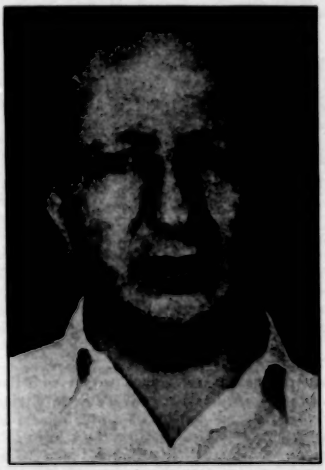

Fig. 8.—Patient V. S.

and Cooley's erythroblastic anemia. In all of these conditions there is found evidence of increased blood destruction and increased but faulty blood formation leading to hyperplasia of the bone marrow and often accompanied by characteristic changes in the bones. It is of interest that these are the only hemopoietic disorders in which pronounced abnormalities in corpuscular resistance to hemolysis have been demonstrated.

In the disorder we have described, thin, pale red corpuscles very resistant to the hemolytic action of hypotonic saline solutions contrast with the thick, dark spherocytes extremely sensitive to hypotonic solutions which are characteristic of familial hemolytic icterus. In the one condition there is only slight evidence of hemolytic anemia, in the other marked blood destruction is characteristic. Both conditions are familial and in both evidence of active erythropoiesis is found.

In sickle cell anemia, as in the blood of our patients, thin and pale and target corpuscles are found [5] and there may be increased resistance of the red cells to hypotonic saline solution.[6] There is hemolytic anemia of variable degree and accompanying this is found evidence of active blood regeneration (erythroblastosis, reticulocytosis, stippling, polychromatophilia, osteoporosis) and splenomegaly (some cases). A benign form, the sickle cell trait, is well recognized. It is a curious fact that, of the five acceptable families of sickle cell anemia in white persons,[5] four were of Greek, Italian or Sicilian parentage. Sickling was repeatedly looked for in wet films of the blood of our patients but was never found.

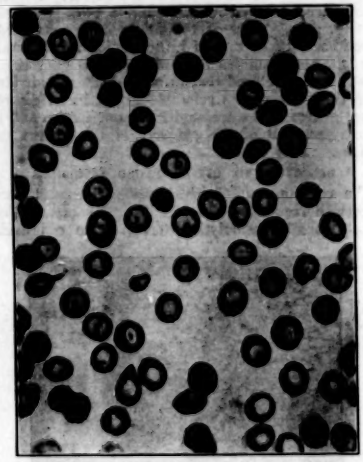

Fig. 9.—Stained smear of blood of patient B. G., showing marked hypochromia, poikilocytosis and target cells. Oil immersion, × 800.

Closest parallelism is found, however, with the condition which Cooley [1] described in Greek, Syrian and Italian children and which has since become known by his name or by the designations erythroblastic anemia, Mediterranean disease and thalassemia.[2] In the typical case of Cooley's anemia there is found erythroblastosis out of all proportion to the severity of the anemia, reticulocytosis, hypochromia, leukocytosis and some evidence of increased blood destruction as well as splenomegaly and even hepatomegaly, a peculiar facial appearance which is described as mongoloid, and increased porosity of the medullary portion of the bones as well as perpendicular hairlike striations in the calvarium. In many instances, more than one child in a family has been affected.[7]

Examination of reports of cases of Cooley's anemia reveals a number of important features of the disease which have received no emphasis. The degree of erythroblastosis is variable, and in some of the reported cases which were typical in all other respects few or no nucleated cells were found.[8] Stippling [9] and polychromatophilia also occur. The anemia is hypochromic and microcytic,[10] yet it fails to respond to iron therapy.[10] Extreme poikilocytosis is common [1] and, although they have received no special attention, target corpuscles are shown in illustrations of the blood in Cooley's anemia.[11] Furthermore, although it is often stated that the fragility of the red corpuscles is normal or only slightly decreased in this disease,[12] examination of case reports reveals that the resistance of the cells to hemolysis has often been found to be greatly increased. Thus Cooley and Lee [13] and Baty, Blackfan and Diamond [14] independently noted that in some instances hemolysis was incomplete even in distilled water. Recently Caminopetros [15] emphasized the significance of this phenomenon and reported increased resistance in all of his thirty-five cases, whereas this was found in none of forty-five cases in which other diseases were present. Finally, the mongoloid facies is not always found.[15]

When this more complete picture of Mediterranean disease is taken into consideration, there appears to be great similarity between the disorder discovered in our cases and that found in thalassemia. These conditions have in common their incidence among the peoples residing on the northeastern shores of the Mediterranean, their familial occurrence, the hypochromia and microcytosis resistant to iron therapy, pronounced stippling, target cells, increased resistance of the red corpuscles to the hemolyzing effects of hypotonic solutions, and bone marrow hyperplasia.

Cooley's anemia differs from the condition observed in our cases in that it occurs in children, the anemia is severe and usually fatal, leukocytosis is common, and characteristic changes in the bones as well as a mongoloid facies have been described.

It seems probable, however, that these are merely differences in degree rather than in the fundamental

6. Diggs, L. W., and Bibb, Juanita: The Erythrocyte in Sickle Cell Anemia: Morphology, Size, Hemoglobin Content, Fragility and Sedimentation Rate, J. A. M. A. **112**:693-700 (Feb. 25) 1939.

7. Péhu, M.; Nové-Josserand, Leon, and Noël, R.: Anémie type Cooley observée à Lyon, chez deux sœurs, nées de parents sardes, Rev. franç. de pédiat. **11**:390-403, 1935. Santillana, A.: Contribution à l'étude de l'anémie de von Jaksch-Luzet à forme familiale du type Cooley, Arch. de méd. enf. **11**:356-368 (June) 1938. Cooley, Witwer and Lee.[1] Hitzrot.[9] Wollstein and Kreidel.[11] Whipple and Bradford.[9] Baty.[14] Koch and Shapiro.[12] Ortolani.[9] Caffey.[13]

8. Kato, Katsuyi, and Downey, Hal: Hematology of Erythroblastic Anemia (Type Cooley), Folia haemat. **60**:35-67, 1933. Cooley, Witwer and Lee.[1]

9. Capper, Aaron: Nature of von Jaksch's Anemia and Effect of Splenectomy, Am. J. M. Sc. **181**:620-629 (May) 1931. Wollstein and Kreidel.[11] Kato and Downey.[8] Baty, Blackfan and Diamond.[14] Hitzrot.[9]

10. Whipple, G. H., and Bradford, W. L.: Mediterranean Disease—Thalassemia (Erythroblastic Anemia of Cooley): Associated Pigment Abnormalities Simulating Hemochromatosis, J. Pediat. **9**:279-311 (Sept.) 1936.

11. Wollstein, Martha, and Kreidel, K. V.: Familial Hemolytic Anemia of Childhood—von Jaksch, Am. J. Dis. Child. **30**:115-130 (Jan.) 1930. Holt, L. Emmett, and Howland, John: Holt's Diseases of Infancy and Childhood, revised by L. Emmett Holt Jr. and Rustin McIntosh, ed. 10, New York, D. Appleton-Century Company, Inc., 1936, p. 533, fig. 88. Baty, Blackfan and Diamond.[14]

12. Koch, L. A., and Shapiro, Benjamin: Erythroblastic Anemia; Review of Cases Reported Showing Roentgenographic Changes in Bones and Five Additional Cases, Am. J. Dis. Child. **44**:318-335 (Aug.) 1932. Caffey.[13]

13. Cooley, T. B., and Lee, Pearl: Erythroblastic Anemia; Additional Comments, Am. J. Dis. Child. **42**:705-708 (March) 1932.

14. Baty, D., Blackfan, K. D., and Diamond, L. K.: Blood Studies in Infants and in Children; Erythroblastic Anemia; Clinical and Pathologic Study, Am. J. Dis. Child. **45**:667-704 (March) 1933; correction **48**:1221 (May) (part 1) 1934.

15. Caminopetros, J.: Recherches sur l'anémie érythroblastique infantile des peuples de la Méditerranée orientale; étude nosologique, Ann. de méd. **42**:27-61 (Jan.) 1938; Recherches sur l'anémie érythroblastique infantile des peuples de la Méditerranée orientale; étude anthropologique, étiologique et pathogénique; la transmission héréditaire de la maladie, ibid. **42**:104-123 (Feb.) 1938.

character of the two disorders. It is likely that the typical cases of Cooley's anemia are extreme examples of the disease and that when the disorder is less severe the patients may reach adult life. We have been able to find reports of seven cases [15a] in persons over 14 years of age which undoubtedly are instances of Cooley's anemia: namely the case of Mandeville,[16] age 15; that of Dalla Volta,[17] age 30, in which considerable iron pigment was found in the organs, and large cells suggesting the foam cells described by Whipple and Bradford in Cooley's anemia [2] were noted; three cases reported by Aravantinos and Delijannis,[18] ages 21, 16 and 22; a case of Allen and Childs,[19] age 24; two cases (5 and 14) reported by Caminopetros,[15] ages 14 and 16, and one recently described by Thalheimer, Mezzeti and Gershon-Cohen,[20] age 14. Nine other cases in adolescents or adults have been reported, but the data presented are insufficient to permit independent appraisal of the diagnosis. These are the cases of Hitzrot,[21] age 14; Baty, Blackfan and Diamond,[14] case 18, age 17; Dalla Volta,[17] age 23; Ortolani,[22] age 30; Caminopetros,[15] cases 12 and 13, ages 21 and 23; Pontoni,[23] age 14; Signorelli,[24] two cases, ages 15 and 21. One case which has been cited [20] as an example of survival into adult life is that of Stillman,[25] whose patient was known to have been living at 25 years of age.[14] The case is not typical, however, for the corpuscular fragility was found to be increased (beginning hemolysis at 0.62 per cent, complete hemolysis at 0.44 per cent) rather than decreased, and great improvement followed splenectomy.

When the patients survive to adolescence or adult life, the blood changes have usually been less marked than in classic cases of Cooley's anemia. The lack of leukocytosis, bone changes and mongoloid facies in our cases may be explained on the assumption that these abnormalities may be expected to vary in degree according to the severity of the underlying disturbance.

Cooley's anemia is considered to be familial but it has not been shown to be hereditary. In the reports of cases of this disease the statement is commonly made that the parents are well,[26] but no complete examinations have been recorded to support this conclusion. It is noteworthy that Caffey [26] expressed the opinion that mild cases occur and that adults with the disease in mild form might transmit the disorder to their offspring. Yet, he stated, he had never found the slightest evidence of erythroblastic anemia, either clinical, hematologic or roentgenologic in the parents of his erythroblastic infants and children.

Recently, however, several Greek and Italian authors, stimulated by Cooley's observations on their compatriots in the United States, have reported extensive studies on members of the families of patients with erythroblastic anemia which afford evidence that this condition is hereditary and that there may be a benign and latent form of the disorder which causes no symptoms and can be recognized only by finding in the blood of such individuals changes similar to those found in Cooley's anemia.

Angelini,[27] in a study of twenty-six members of six families, found that nearly all parents and siblings showed two striking features, namely slightly increased bilirubinemia and well marked increase in erythrocyte resistance to hemolysis. Caminopetros [15] found thirty-five cases of erythroblastic anemia in eastern Greece

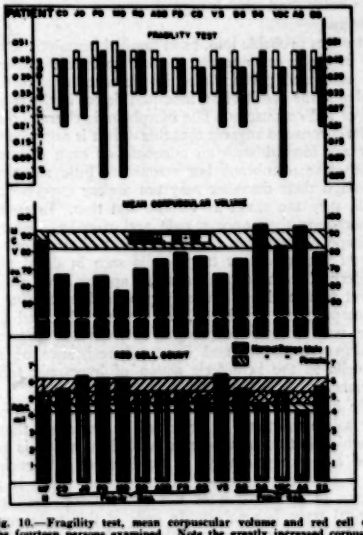

Fig. 10.—Fragility test, mean corpuscular volume and red cell count in the fourteen persons examined. Note the greatly increased corpuscular resistance to the hemolyzing effects of hypotonic saline solution, the microcytosis and the normal or high red cell counts in many of the cases. In the fragility tests the control test on normal blood is indicated by open rectangles, whereas the results for each patient are indicated by the hatched and black rectangles. The hatching represents slight hemolysis, the black represents marked hemolysis. The point at which hemolysis was marked in the controls is indicated by a horizontal line. The red cell count of males is indicated by solid black rectangles, that of females by open rectangles. The column marked *N* indicates the normal.

and made detailed observations on several generations of four families. In one of these there were as many as ten probable cases of erythroblastic anemia in four generations. In addition, in apparently well members of these families increased corpuscular resistance as well as slight bone changes were demonstrated. It is noteworthy that, in fifteen cases in which data were available for both parents, increased corpuscular resistance was observed in both parents in seven instances and in one parent in the remainder. Caminopetros concluded that the erythrocyte anomaly is a recessive transmitted according to the mendelian law.

15a. Since this article was written, two additional cases have been described by D. W. Atkinson (Am. J. M. Sc. **198**: 376 [Sept.] 1939). The patients were a sister and brother aged 20 and 17 years respectively.

16. Mandeville, F. B.: Roentgen Ray Findings in Erythroblastic Anemia, Radiology **15**: 72-84 (July) 1930.

17. Dalla Volta, Alessandro: Splenomegalia emolitica famigliare eritremica (sindrome di Cooley), Arch. di pat. e clin. med. **15**: 34-74, 1935.

18. Aravantinos, A., and Delijannis, G.: Ueber das Auftreten der Erythroblastenanämie bei Erwachsenen, Klin. Wchnschr. **15**: 1792-1797 (Dec. 5) 1936.

19. Allen, E. G., and Childs, D. S.: Erythroblastic Anemia, New York State J. Med. **36**: 641-645 (April 15) 1936.

20. Thalheimer, E. J.; Mezzeti, Alfred, and Gershon-Cohen, Jacob: Cooley's Anemia (Mediterranean Anemia) with Report of a Case in an Adolescent, J. Pediat. **14**: 349 (March) 1939.

21. Hitarot, J. M.: Unclassified Type of Splenomegaly in Children, Ann. Surg. **88**: 361-379 (Sept.) 1928.

22. Ortolani, M.: L'anemia di Cooley in gemelle monocorie, Lattante **7**: 323 (July), 375 (Aug.) 1936.

23. Pontoni, L.: Aspects cliniques et pathogéniques de l'erythrémie chronique familiale, type Cooley, Rev. belge sc. méd. **10**: 216-226 (April) 1938.

24. Signorelli, quoted by Pontoni.[23]

25. Stillman, R. G.: A Study of von Jaksch's Anemia, Am. J. M. Sc. **152**: 218-231 (Feb.) 1917.

26. Caffey, John: Skeletal Changes in Chronic Hemolytic Anemias (Erythroblastic Anemia, Sickle Cell Anemia and Chronic Hemolytic Icterus), Am. J. Roentgenol. **37**: 293-324 (March) 1937. Cooley, Witwer and Lee.[1]

27. Angelini, Valentino: Primi risultati di ricerche ematologiche nei familiari di ammalati di anemia di Cooley, Minerva med. **2**: 331-332 (Sept. 30) 1937.

NATURE OF THE HEMOPOIETIC DISORDER

We are inclined to believe that the cases described represent a benign and latent form of the condition first differentiated by Cooley under the title of erythroblastic anemia but later called Mediterranean disease or thalassemia by Whipple and Bradford,[10] who thought that anemia alone is not a diagnostic factor in this disorder and need not be emphasized. Our view would be more convincing if at least one well marked instance of Cooley's anemia had been observed in the families we have studied.[28] The hypothesis is supported, however, by the descriptions which have appeared lately of less severe cases with survival to adolescence and even adult life, and by the families in Greece studied by Caminopetros [15] and others which seem to represent grades of severity between the fatal anemia described by Cooley and the benign condition found in our patients.

It seems probable that, as in familial hemolytic icterus and in sickle cell anemia, the hemopoietic disorder in our cases and perhaps also in the cases described by Cooley is the result of an inherited defect in the formation of red corpuscles. The morphologic characteristics of the corpuscles suggest that this defect is one whereby they are formed with an adequate or even excessive corpuscular membrane but containing little substance. Although their diameter may not appear exceptionally small, they are small in volume and thin. In stained preparations they appear pale and ringlike, distorted in shape or resemble targets. Recent observations by Barrett [2] indicate that target cells seen in dried films are derived from corpuscles which appear bowl shaped in wet films and are probably produced by folding of the corpuscular membrane. He further observed that there was a close correlation between the presence of target corpuscles and increased resistance of the red cells to the hemolytic action of hypotonic saline solutions.

The increased resistance of the corpuscles to hypotonic saline solutions is explained by assuming that a cell which is thin is similar to a bladder which is collapsed and almost empty: as fluid passes into such a cell, it gradually becomes distended but there is no increase in the tension of the cell envelop until the spherical stage is reached. In cells of this type much more fluid needs to be absorbed to produce the spherical shape and the bursting point than in the case of normal cells. This concept is in keeping with the observations of Haden [29] and others,[30] who have shown that differences in the susceptibility of various types of erythrocytes to hemolysis are due largely to differences in form.

The other characteristics of this disorder can be explained by the assumption that they are due to attempts to compensate for the faulty red cell formation. Many cells are produced (erythrocytosis), immature cells appear in the blood (stippling, polychromatophilia, erythroblastosis), the bone marrow becomes hyperactive (erythroblastosis) and osteoporosis occurs (x-ray observations), and splenomegaly develops. The bilirubinemia and urobilinuria found in these cases are not readily explained. It is perhaps noteworthy that a few small, dark red corpuscles resembling the fragile spherocytes of hemolytic jaundice were found in the blood of one of our patients (M. D.) and in several members of the two families studied (table 2).

The cause of the defect is obscure. Whipple and Bradford [10] expressed the opinion that Mediterranean disease may be a metabolic disorder or a deficiency disease which results in disturbed erythropoiesis as well as in faulty bone and bodily development and deposition of pigment in the tissues. Others,[21] noting the retardation of growth observed in cases of Cooley's anemia [10] and the infantilism found in some older patients,[22] have sought to attribute the disease to an endocrine disorder. At the present time these views are purely speculative.

SUMMARY

Fourteen individuals, members of three Italian families representing three generations in one family and two in another, have been examined and have been found to have certain abnormalities.

In four, marked poikilocytosis, microcytosis, hypochromia and stippling of the red cells as well as corpuscles resembling targets were observed. In addition there were increased resistance of the red corpuscles to the hemolytic action of hypotonic saline solutions, splenomegaly and bilirubinemia or urobilinuria. One of these patients also had erythroblastosis in the sternal bone marrow and slight osteoporosis.

In four instances all of the abnormalities mentioned except splenomegaly were found. In two children there was slight splenic enlargement without significant changes in the blood. Of the remaining four persons, all females, there was microcytosis without other significant changes in two, and slight macrocytosis as well as stippling in two.

This disorder may be considered to be a benign form of Cooley's anemia or Mediterranean disease.

This condition and Cooley's anemia appear to be the result of an inherited defect in the production of red corpuscles whereby corpuscles are formed with an adequate or excessive membrane which contains little substance. As a result the cells can withstand the hemolyzing effect of hypotonic saline solutions more readily than normal cells. The other characteristics of the disorder are explained by the assumption that they are due to attempts to compensate for the faulty red cell formation.

28. Such confirmation has now been obtained. Since completion of this paper we have had an opportunity to study an Italian child with typical Cooley's anemia, as well as her father and mother. The child showed all the characteristics already described. The mother's spleen is palpable. Both parents have slight anemia (father's hemoglobin 11.6 Gm., mother's hemoglobin 9.5 Gm.) of the hypochromic microcytic type and show marked poikilocytosis as well as moderate numbers of stippled and target corpuscles. In hypotonic saline solutions, hemolysis of the father's red cells is complete only at 0.21 per cent, the mother's corpuscles at 0.03 per cent.

29. Haden, R. L.: The Mechanism of the Increased Fragility of the Erythrocytes in Congenital Hemolytic Jaundice, Am. J. M. Sc. **188**: 441-449 (Oct.) 1934.

30. Castle, W. B., and Daland, G. A.: Susceptibility of Mammalian Erythrocytes to Hemolysis with Hypotonic Solutions: A Function of Differences Between Discoidal Volume and Volume of a Sphere of Equal Surface, Arch. Int. Med. **60**: 949-966 (Dec.) 1937.

31. Lehndorff, H.: Die Erythroblastenanämie, Ergebn. d. inn. Med. u. Kinderh. **50**: 568-619, 1936.

32. Dalla Volta.[31] Aravantinos and Delijannis.[33] Caminopetros.[15]

Airsickness.—That airsickness is produced principally by motion (more specifically by acceleration) is indicated by two well known facts. The first of these is that the frequency of airsickness and its severity, where it does occur, is in direct proportion to the amount and duration of the accelerations encountered in flight. The second is that persons with dead labyrinths seldom if ever become airsick. This latter would seem to confirm the general impression that airsickness is entirely an internal ear problem and simply a particular form of vertigo.—Armstrong, Harry G.: Principles and Practice of Aviation Medicine, Baltimore, Williams & Wilkins Company, 1939.

THE BIOLOGIC EFFECTS OF ANDROGEN (TESTOSTERONE PROPIONATE) IN WOMEN

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In the past year several publications have appeared reporting the use of synthetic androgen (testosterone propionate) in functional gynecologic conditions.[1] The therapeutic results in many cases have been striking, and the question arises as to whether the use of androgen in women is to be considered as purely empiric or as a form of hormonal substitution therapy, correcting a preexisting deficiency. It is of considerable importance, therefore, to know what the biologic properties of androgen are in women. Unfortunately, the majority of the reports on the use of this substance in women consist of purely clinical studies. However, in a few instances attempts were made to determine objectively the biologic effects of male hormone administered to women. Thus it has been shown that testosterone propionate inhibits the gonadotropic hyperactivity of the hypophysis of a castrate woman,[2] suppresses menstruation,[3] produces atrophy of the endometrium [4] and at the same time induces estrogen deficiency changes in the vaginal smear [5] with disappearance of the glycogen;[6] it also inhibits peristalsis of the fallopian tubes.[7] In addition, it has been noted that in some women signs of virilism appear during the course of treatment with testosterone; viz., enlargement of the clitoris,[8] acne, hoarseness and hirsutism.[9] Because of the fact that testosterone propionate can produce such striking somatic effects in women and in view of the current interest in testosterone as a therapeutic agent, we report our experience with the use of testosterone propionate in a series of twenty-five women with normal menstrual cycles. This group was selected out of a larger group of 153 women that have been treated with testosterone propionate during the past two and one half years.

The large group consisted of patients with functional menometrorrhagia, menometrorrhagia associated with fibroids, endometriosis, functional dysmenorrhea, mastalgia and premenstrual tension. The results of our experience with testosterone propionate as a therapeutic agent in the treatment of functional bleeding (Geist, Salmon and Gaines [9]) and dysmenorrhea [10] have already been reported. Reports on the other conditions will be published. Here we will describe the biologic effects of different doses of testosterone propionate administered over varied periods of time to women with regular menstrual cycles.

THE MALE SEX HORMONES (ANDROGENS)

Because of the recent developments in the chemistry of the steroid sex hormones, new terms have been introduced to designate the different compounds of male sex hormone that have been identified. The term "androgen" is used to designate all compounds that have the characteristic properties of male sex hormone in contradistinction to the estrogens, which are female sex hormones. Three androgens have been found to exist in the organism, androsterone, transdehydro-androsterone and testosterone. The last-mentioned androgen is believed to be the physiologically active substance found in the testes, and the first two are the excretory forms found in the urine. A large variety of androgenic compounds, including testosterone, have been synthesized in the past three years. It has further been found that the activity of testosterone is greatly increased by esterification.[11] The propionic acid ester of testosterone is considered to be the most active androgen and has been used almost exclusively in our clinical studies.

EFFECT OF TESTOSTERONE PROPIONATE ON FEMALE ANIMALS

That pure male hormones have bisexual activity, simulating in some respects the effect of estrogens in female animals, was reported by Butenandt and Kudzus,[12] Korenchevsky, Dennison and Simpson [13] and Deanesly and Parkes.[14] The estrogen-like properties of the male sex hormones were attributed to their close chemical relation to the estrogenic hormones. It was subsequently shown by Salmon that not only do androgens exercise a direct stimulating effect on the müllerian tract of rats but they also produce follicle growth and corpora lutea in the ovaries of immature rats.[15] Nathanson, Franseen and Sweeney have shown that this gonadotropic effect is mediated through the hypophysis.[16] Furthermore, progestational changes have been produced in the endometrium of rabbits [17] with testosterone and in spayed rats with testosterone propionate.[18] There is evidence, therefore, confirmed in several laboratories, that androgens actively stimulate growth of the muscular and epithelial components of the genital tract of intact, as well as of spayed, immature and mature rodents.

In contrast to these experiments, observers have reported that androgens suppress estrous phenomena in

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The following pharmaceutic houses supplied the testosterone propionate used in this study: Ciba Pharmaceutical Products, Inc., Summit, N. J., (perandren) and the Schering Corporation, Bloomfield, N. J., (oreton).

1. Desmarest, E., and Capitaine, Mme.: Presse méd. **46**: 185 (Feb. 5) 1938. Loeser, A. A.: Lancet **1**: 373 (Feb. 12) 1938. Salmon,[5] Geist and others.[9] Foss.[8]
2. Salmon, U. J.: Proc. Soc. Exper. Biol. & Med. **37**: 488 (Dec.) 1937.
3. Papanicolaou, G. N.; Ripley, H. S., and Shorr, Ephraim: Proc. Soc. Exper. & Med. **37**: 689 (Jan.) 1938. Gaines and others.[4]
4. Gaines, J. A.; Salmon, U. J., and Geist, S. H.: Proc. Soc. Exper. Biol. & Med. **38**: 279 (June) 1938. Papanicolaou and others.[3]
5. Papanicolaou and others.[3] Salmon and others.[6]
6. Salmon, U. J.; Walter, R. I., and Geist, S. H.: Proc. Soc. Exper. Biol. & Med. **39**: 467 (Dec.) 1938.
7. Geist, S. H.; Salmon, U. J., and Mintz, Maurice: Proc. Soc. Exper. Biol. & Med. **41**: 556, 1939.
8. Foss, G. L.: Lancet **1**: 992 (April 30) 1938.
9. Geist, S. H.; Salmon, U. J., and Gaines, J. A.: Endocrinology **23**: 784 (Dec.) 1938. Greenhill, J. P., and Freed, S. C.: J. A. M. A. **112**: 1573 (April 22) 1939. Salmon and others.[6]
10. Salmon, U. J.; Geist, S. H., and Walter, R. I.: Am. J. Obst. & Gynec. **38**: 264 (Aug.) 1939.
11. Miescher, Karl; Wettstein, Albert, and Tschopp, Ernst: Biochem. J. **30**: 1970 (Nov.) 1936.
12. Butenandt, A., and Kudzus, H.: Ueber Androstendion, einen hochwirksamen männlichen Pragungsstoff, Ztschr. f. physiol. Chem., Hoppe-Seyler's **237**: 75 (Nov. 9) 1935.
13. Korenchevsky, Vladimir; Dennison, Marjorie, and Simpson, S. L.: Biochem. J. **29**: 2534 (Nov.) 1935.
14. Deanesly, R., and Parkes, A. S.: Brit. M. J. **1**: 257 (Feb. 8) 1936.
15. Salmon, U. J.: Proc. Soc. Exper. Biol. & Med. **38**: 352 (April) 1938; Endocrinology **23**: 779 (Dec.) 1938.
16. Nathanson, I. T.; Franseen, C. C., and Sweeney, A. R., Jr.: Proc. Soc. Exper. Biol. & Med. **39**: 385 (Nov.) 1938. Since the completion of this manuscript, the Mazers have reported that continued administration of testosterone produces degenerative changes in the rat ovary (Mazer, Milton, and Mazer, Charles: Endocrinology **24**: 175 [Feb.] 1939).
17. Klein, M., and Parkes, A. S.: Proc. Roy. Soc., London, s.B. **121**: 574 (Feb. 3) 1937.
18. Korenchevsky, Vladimir, and Hall, Kathleen: J. Path. & Bact. **45**: 681 (Nov.) 1937.

mice [19] and rats,[20] cause inhibition of ovulation in rabbits [21] and monkeys [22] and suppress menstruation in monkeys. [23] It has been assumed, on the basis of the suppression of the estrous cycle (as determined by the vaginal smears), that androgens are antagonists of the estrogens. On the other hand, as Korenchevsky and his co-workers have shown, the vaginal smear studies are misleading in regard to the action of androgens in female animals, since testosterone causes mucification of the vagina.[24]

Fig. 1.—Preliminary premenstrual biopsy section showing secretory phase.

As one surveys the literature, one is impressed with the protean character of the androgenic effects in animals. The effects of androgens seem to vary, depending on the type of androgen, the dosage, the duration of the injections and the age and species of the animals. It does not fall within the province of this report to attempt to correlate the vast amount of work which has been reported in this field. However, this brief review will suffice to indicate that the observations and conclusions derived from animal experimentation with testosterone propionate cannot as yet be applied to the human female.

EXPERIMENTAL PROCEDURE

The ages in the twenty-five cases reported here varied from 16 to 37 years. The preliminary study consisted of a general physical and gynecologic examination, a vaginal biopsy, a vaginal smear and a premenstrual endometrial (suction) biopsy. In all of these cases the premenstrual endometrial biopsies revealed a typical secretory phase indicating a normal ovarian cycle (fig. 1), the vaginal mucosa a normal cornification and layering, and the smears a normal characteristic estrogen effect (fig. 4). The vaginal smears were prepared and stained with fuchsin, as previously described.[25]

An attempt was made to determine whether variations in dosage or in time of administration influenced the results. The dose administered varied from 60 to 1,000 mg. a month. The androgen was administered intramuscularly in sesame oil in individual doses varying from 10 to 100 mg. In the majority of cases injections were given three times weekly throughout the month; in others the androgen administered was concentrated in the first ten to fourteen days of the cycle, and in still others similar amounts were given only during the latter half of the cycle. Endometrial and vaginal biopsies, as well as vaginal smears, were taken at intervals during and after administration of testosterone propionate.

RESULTS

Doses of 500 Mg. or More a Month.—Effect on Menstruation: Menstruation was delayed from one to two weeks or completely suppressed for from four to six weeks in the patients receiving this dosage. When menstruation occurred, the flow was often diminished in amount. Thereafter the normal menstrual rhythm was reestablished.

Fig. 2.—Endometrial biopsy section after the administration of 650 mg. of testosterone propionate, showing atrophy.

Effect on Endometrium: The endometrium at the end of a month of treatment showed absence of the secretory phase and, in most cases, subnormal prolifera-

19. Robson, J. M.: Proc. Soc. Exper. Biol. & Med. **35**: 49 (Oct.) 1936.
20. Browman, L. G.: Proc. Soc. Exper. Biol. & Med. **36**: 205 (March) 1937. Nelson, W. O., and Merckel, C. G.: ibid. **36**: 823 (June) 1937.
21. Cotte, G., Martin, J. F., and Mankiewicz, E.: Gynécologie **36**: 561 (Oct.) 1937.
22. Zuckerman, S.: Lancet **2**: 676 (Sept. 18) 1937.
23. Hartman, C. G.: Proc. Soc. Exper. Biol. & Med. **37**: 87 (Oct.) 1937. Zuckerman.[22]
24. Korenchevsky, Vladimir; Dennison, Marjorie, and Hall, Kathleen: Biochem. J. **31**: 780 (May) 1937.
25. Salmon, U. J., and Frank, R. T.: Proc. Soc. Exper. Biol. & Med. **35**: 612 (Jan.) 1936.

tion. The maximum regressive changes were noted approximately between one and two weeks after the cessation of the testosterone therapy, at which time the endometrium was often found reduced to a state of hypoplasia or atrophy (fig. 2), ordinarily found only

Fig. 3.—Endometrial biopsy section six weeks after discontinuation of testosterone propionate, showing restoration to the normal secretory phase. Menstruation occurred six days later.

many years after the menopause. Signs of regeneration began to appear shortly thereafter. Further endometrial biopsies indicated a rapid restoration of the normal proliferative and secretory pattern within the following three or four weeks.

Effect on Vagina: Doses of 500 mg. or more given throughout one month resulted in regressive changes in the vaginal smear (estrogen deficiency changes) resembling those of the menopause type of smear. The regressive changes began to appear three weeks after the beginning of treatment and thereafter developed very rapidly, so that from five to ten days after the first signs of regression appeared the smears indicated an advanced degree of estrogen deprivation. The normal squamous epithelial cells vanished and were replaced by the small epithelial (atrophy) cells and leukocytes (figs. 5 and 6). Coincidentally with this, the glycogen content of the cells was markedly diminished.

It is interesting to note that within two or three weeks after discontinuation of testosterone the smears began to show rapid regeneration, the epithelial cells became larger, a scattering of squamous epithelial cells began to appear and increased progressively in number, glycogen appeared in increasing amounts in the cells, the leukocytes vanished, and at the end of three or four weeks after the last injection the smear resembled that of a normal adult woman (fig. 7).

Doses of Approximately 300 Mg. a Month.—With doses of 300 mg. a month the effects produced were variable. In some cases menstruation was delayed several days and in others it occurred at the expected time. The flow was usually diminished. In some cases the premenstrual endometrial biopsy showed absence of progestational changes. The vaginal smears in the majority of cases showed no significant changes during the period of testosterone propionate administration. In several cases, however, early regressive signs appeared during the latter part of the course of treatment and in some instances for a few days following the next menstrual period.

Doses of 200 Mg. or Less a Month.—With this dosage no demonstrable changes were noted in the endometrium or vaginal smears. The periods occurred at the expected time but in some of the patients the flow was slightly diminished. In several cases menstruation occurred from three to seven days prematurely and was associated with slight increase in bleeding.

Testosterone Propionate Administered During First Two Weeks of the Cycle.—In the cases in which testosterone propionate was given only during the first ten to fourteen days of the cycle (beginning with the first day of menstruation) in doses of from 300 to 500 mg. menstruation was delayed from one to four weeks, and this was usually associated with inhibitory effects on the endometrium and vaginal smears. Similar amounts administered during the last two weeks of the cycle caused neither delay in menstruation nor demonstrable changes in the smears in the current month.

Fig. 4.—Preliminary vaginal smear showing normal estrogenic effect (large squamous epithelial cells with small nuclei).

Androgenic Effects (Virilism).—In addition to the morphologic effects on the genital tract just described, some interesting clinical effects were noted in some of the cases in which the very large doses (500 mg. or more a month) were given. These were slight facial hirsuties, hoarseness and acne. It is interesting to note

that these signs and symptoms appeared singly in some cases and in combination in others.

In view of the clinical importance of these effects, we report here the side effects noted in the larger series of 153 women who were treated with testosterone propionate for dysmenorrhea, functional bleeding, mittelschmerz, mastalgia, premenstrual tension and menopausal syndrome. The monthly dose in these cases varied from 40 to 1,200 mg. The total dose administered to individual patients (during periods extending from one to seven months) varied from 40 to 2,150 mg. The incidence of androgenic phenomena in this series was hypertrichosis 11 per cent, voice changes 13 per cent and acne 8 per cent.

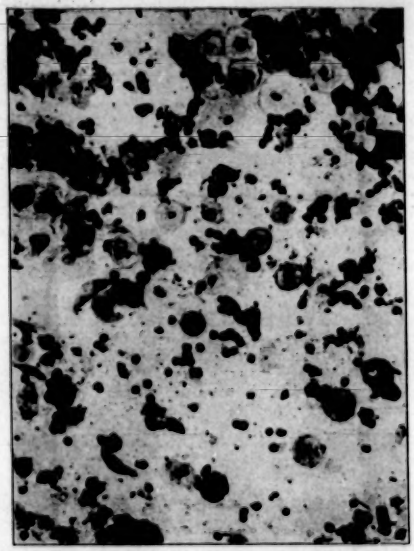

Fig. 5.—Vaginal smear following the administration of 600 mg. of testosterone propionate. The smear reveals signs of estrogen deficiency, manifested by the disappearance of large squamous epithelial cells and appearance of numerous small round epithelial cells (atrophy cells) and leukocytes.

Hypertrichosis: We characterized as hypertrichosis any growth of hair on the upper lip or chin regardless of how slight in degree. In four cases there was also an increased growth of hair on the arms and legs, in two also on the lower abdomen, and in several a few hairs appeared on the areolas of the breasts.

It is significant that in all but two cases in which hirsutism developed more than 500 mg. was given. In the majority of these the individual dosage exceeded 900 mg. In only two cases of the entire series was hirsutism produced with less than 500 mg. (in one case with 315 mg. and in the other with 450 mg.). The hirsuties was very slight in degree in both these cases. Brunets, particularly those with preexisting hypertrichosis, appeared to be most susceptible. The hirsuties began to appear usually from five to six weeks after the beginning of testosterone administration. In approximately 60 per cent of these cases the hirsuties disappeared within several months after discontinuation of treatment; the remaining cases showed varying degrees of progressive improvement. In two cases there was still slight hypertrichosis as late as fourteen months after the discontinuation of testosterone. Both these patients received extremely large doses (2,150 and 1,975 mg.).

Voice Changes: In 13 per cent of the patients some changes in their voices developed during or after the administration of testosterone. The majority of these consisted of hoarseness, which the patients ascribed to a "cold." Some patients complained of a feeling of "tightness in the throat." Two thirds of the patients were completely restored to normal. The others retained a slightly lowered pitch or husky quality which continued to improve under observation, to date. It is noteworthy that only three of the patients receiving less than 500 mg. (470, 315 and 425 mg.) had some hoarseness, and these were all restored to normal.

Acne: The acne which occurred was usually mild and consisted of scattered papules on the face and chest. In some cases the acne was induced with relatively small doses, in one instance as small as 150 mg. The acne disappeared rapidly within five to ten days after discontinuation of treatment.

In only two cases was an appreciable enlargement of the clitoris observed. The enlargement persisted but caused no symptoms.

Estrogen Deficiency Phenomena: Some of the patients receiving sufficiently large doses to produce regressive changes in the vaginal smear complained of vaginal discomfort and/or pruritus vulvae. Examination revealed mild atrophic vaginitis. The symptoms disappeared within a few weeks after discontinuation of treatment. A few of these patients complained of flushes which developed during the period of induced

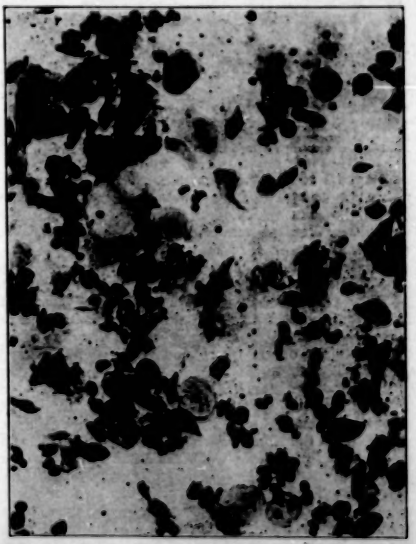

Fig. 6.—Vaginal smear ten days after discontinuation of treatment. The smear still shows the effect of testosterone propionate.

amenorrhea. These flushes disappeared, usually coincidently with the restoration of the vaginal smear to a normal status.

COMMENT

It is apparent from the observations recorded here that testosterone propionate administered in adequate doses to normally menstruating women suppresses menstruation temporarily and induces a rapidly developing atrophy of the endometrium and vagina. The question arises as to the mechanism of the testosterone action. It has been shown that androgen administered to a castrated rat prevents the postcastration changes in the hypophysis [26] and that the excretion of gonadotropic substance by a castrated woman can be suppressed with testosterone propionate.[2] It seems not illogical to assume that a similar inhibition of the gonadotropic activity of the hypophysis occurred in the cases reported here. This explanation is supported by the observation that testosterone propionate administered during the first two weeks of the cycle (in time to inhibit the secretion of gonadotropic substance by the hypophysis) will suppress or delay menstruation, whereas similar amounts administered during the latter half of the cycle (after ovulation has occurred) will have no such effect. As a result of this inhibition, the normal gonadotropic stimulation of the ovaries fails to occur, ovulation is consequently suppressed and the normal formation of estrogen and progesterone is inhibited. This is revealed in failure of the normal proliferative and progestational changes of the endometrium to appear and in the atrophy of the vaginal mucosa. Inhibition of estrogen formation in the ovary, however, does not satisfactorily explain the rapid development of the signs of estrogen deficiency (atrophy of the endometrium and vaginal mucosa), since such advanced signs of atrophy do not usually appear until many months after bilateral oophorectomy or the menopause. This suggests an actual inactivation of the available stored estrogens or of estrogens circulating in the body.

It appears that if large doses of testosterone propionate are given there develop morphologic signs and clinical symptoms indicative of an estrogen deficiency. Thereafter in some of the women signs and symptoms develop which one may regard as androgenic, viz. amenorrhea, hirsutism, hoarseness, acne and enlargement of the clitoris—a syndrome which is reminiscent of arrhenoblastoma of the ovary or tumors of the adrenal cortex. After discontinuation of the testosterone, a restoration to normal status of the menstrual rhythm and of the histologic pattern of the endometrium and vagina occurs, and the signs of virilism recede gradually.

It should be emphasized that both estrogenic deficiency and androgenic signs and symptoms were usually produced with large doses (500 mg. or more a month), whereas doses of less than 300 mg. produced no untoward effects.

A significant fact that emerges from this study is the sensitiveness of the vaginal smear as an indicator of androgenic effect. The smear will frequently reveal early regressive changes after the administration of amounts of testosterone which are insufficient to inhibit menstruation or produce masculinization phenomena. For this reason it is exceedingly important to take vaginal smears at frequent intervals while the testosterone is being administered. Signs indicative of estrogen deficiency in the smear should serve as a warning to discontinue treatment.

It has been shown that normal adult women excrete significant amounts of androgens (an average of 26 international units a day), whereas before puberty the androgen excretion is extremely small (from 1.8 to 2 international units per liter).[27] This fact, coupled with the striking inhibitory effects produced by testosterone on the endometrium and vaginal mucosa, suggests that androgens may play a definite role in the sex hormone metabolism of the female. We have previously suggested that androgens probably modify or restrain the action of the estrogens and that in the normal woman

Fig. 7.—Vaginal smear taken twenty days after discontinuation of testosterone propionate, showing restoration to normal. Menstruation occurred ten days later.

there is a balance between the estrogens and the androgens.[10] The therapeutic results obtained with testosterone propionate in menometrorrhagia and dysmenorrhea suggest that in these conditions there may be some abnormality in the androgen metabolism so that the normal balance may be upset.

SUMMARY AND CONCLUSIONS

1. The effects of testosterone propionate were studied in a series of twenty-five women with normal menstrual cycles. Endometrial biopsies and vaginal smears were taken before, during and after administration of androgen.

2. Testosterone propionate in doses of 500 mg. or more a month produced (*a*) temporary suppression of menstruation, (*b*) hypoplasia or atrophy of the endometrium and (*c*) evidence of estrogen deficiency in the vaginal smear. Restoration to normal occurred in all cases after cessation of treatment.

26. Reese, J. D., and McQueen-Williams, M.: Am. J. Physiol. **101**: 239 (July) 1932. Nelson, W. O., and Gallagher, T. F.: Anat. Rec. **54**: 129 (Dec.) 1933. Wolfe, J. M., and Hamilton, J. B.: Proc. Soc. Exper. Biol. & Med. **36**: 307 (April) 1937.

27. Koch, F. C.: Harvey Lectures 1937-1938, Baltimore, Williams & Wilkins Company, 1938, p. 205.

3. Doses of 200 mg. or less a month did not suppress menstruation or cause any demonstrable changes in the endometrium or vaginal smears. With intermediate doses the effects produced were variable.

4. Large doses of testosterone propionate (more than 500 mg. a month) may produce the following symptoms and signs: (*a*) signs of estrogen deficiency, including temporary amenorrhea and senile vaginitis, and (*b*) androgenic effects, including hoarseness, hirsuties, acne and enlargement of the clitoris. In almost all cases these phenomena regress spontaneously after discontinuation of treatment.

5. It is suggested that the mechanism of testosterone action is threefold: (*a*) inhibition of the gonadotropic factors of the hypophysis resulting in failure of ovulation and suppression of the normal formation of estrogen and progesterone, (*b*) direct inactivation of the available estrogens in the body, and (*c*) the production of androgenic effects (virilism).

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ABSTRACT OF DISCUSSION

Prof. Ernst Laqueur, Amsterdam, Netherlands: A few historical remarks about the influence of testosterone on female organs may be of interest. Fourteen years ago estrogens were injected in the form of extracts from follicle fluids into castrated mice and tried the effect of testicular extracts on the estrous reaction. The idea was that testicular extracts might have an inhibiting effect on estrus. The experiment proved that the idea was wrong, because estrus was not inhibited. The estrogenic effect was rather enhanced by extracts of testis and estrogenic substances were found in this male organ; some years later Koch with his associates in America found a male substance in testicles. When making extracts from testicles was resumed the same thing was found and four years ago testosterone was identified. I believe that the original idea of Dr. Moore in Chicago was that sex hormones inhibit the hypophysis and that under such circumstances the gonadotropic influence of the hypophysis on the ovaries is eliminated. I did not understand the authors' reasons for inferring a direct antagonism between the sex hormones. I can show on lantern slides the results of my collaborator Dr. Mühlbock. Last year he showed that the effect of androsterone on the comb of the capon is suppressed by estradiol benzoate. It is not known whether this effect is due to some interference with the function of the pituitary. According to another series of experiments the different female substances have a different potency of inhibition on the comb. Estradiol benzoate is more effective than estrone, while estriol has no effect though chemically related to the other two. Progesterone has a similar effect, whereas pregnandiol is without effect. I mention these experiments because they show the importance of the choice of closely allied substances for certain purposes. This is essential from a general point of view, while the details of the experiment are less important.

Dr. Harold S. Connamacher, Newark, N. J.: I should like to ask the authors the method they use in obtaining the vaginal smear.

Dr. Udall J. Salmon, New York: It is an honor to have Professor Laqueur discuss this paper. We are in debt to him for his pioneer work with both the estrogens and the androgens. In answer to his question, we noted that one month after the administration of about 600 mg. of testosterone to a regularly menstruating woman the endometrium and vaginal smears were reduced to an advanced degree of atrophy. If one is to assume that the testosterone produces this effect solely by inhibiting the mechanism of estrogen formation, then one would expect to find similar degrees of atrophy a month or so after removal of both ovaries. But actually of a series of more than a hundred cases of bilaterally ovariectomized women for whom we did vaginal smears and vaginal biopsies from one to twelve months after removal of the ovaries, the majority did not show comparable degrees of atrophy. It appears, therefore, that there must be some other factor, in addition to the estrogen deprivation, to account for the rapid appearance of atrophic changes in the genital tract when testosterone is administered. We accordingly assumed that the testosterone either inactivates whatever estrogens are stored in the body or has a direct inhibitory effect on the uterine and vaginal mucous membrane. It is becoming increasingly more evident that physicians are only beginning to understand the physiologic ramifications of the steroid sex hormones. There is reason to believe that not only the androgens but also the adrenal cortex hormones play an important role in the sex hormone physiology of the female. Thus we have recently found that desoxycorticosterone has an estrogenic effect on women. This seems to indicate that the adrenal cortex may supplement the estrogenic activity of the ovaries and may explain the hitherto puzzling observation that estrogens are excreted after bilateral ovariectomy. The chemists have made brilliant progress in isolating and synthesizing these complex compounds. It is for the biologist and clinician to determine the physiologic properties of these hormones and to define their role with regard to the many unsolved problems in endocrinology. In reply to the question concerning the technic employed for the vaginal smears: The reagent is a 12 per cent aqueous solution prepared from a saturated alcoholic solution of fuchsin. The vaginal secretion is diluted with physiologic solution of sodium chloride, spread on a glass slide, allowed to dry in air and then stained for thirty seconds with the fuchsin solution. It is then washed with tap water and examined.

Clinical Notes, Suggestions and New Instruments

TRAUMATIC RUPTURE OF THE SPLEEN AND THE STOMACH

Melvin A. Casberg, M.D., St. Louis

The success of automotive engineering in its achievement of high speed in transportation has brought with it numerous rather tragic aftermaths, not the least of which is the ever increasing supply of material for the field of traumatic surgery. Though the major portion of such reconstructive effort falls within the realm of fractures, one of the most intriguing parts of this surgical specialty, from the standpoint of diagnosis and treatment, is that of intra-abdominal injury. There are four organs within the abdominal cavity the pulpy structure of which makes them readily susceptible to external injury; the liver, the two kidneys and the spleen.

Splenic rupture may be caused by direct or indirect violence or may occur spontaneously. In the last type of rupture, which is rather uncommon,[1] there is usually some underlying splenic pathologic change such as is observed in the splenomegaly of malaria or a blood dyscrasia. The onset of such an accident is dramatic and without warning, but the symptoms and physical features are similar to those observed in traumatic rupture of the spleen. Open wounds or direct injuries of the spleen are in the majority of cases complicated by injuries to other adjacent viscera,[2] whereas subcutaneous or indirect injuries to the spleen are less frequently so complicated.[3]

Report of Case

The following case was felt to be of sufficient interest for publication because of the complication of an indirect rupture of the spleen by a simultaneous gastric rupture:

J. S., a boy aged 3 years, was brought to the City Hospital Aug. 12, 1939, about one hour after having been struck by a

From the Division of Public Welfare, City Hospital.

1. Haden, R. L., and Dinsmore, R. S.: Indications for Splenectomy, S. Clin. North America **17**: 1391-1398 (Oct.) 1937.

2. Moynihan, Sir Berkeley: Abdominal Operations, Philadelphia, W. B. Saunders Company, 1926, vol. 2, pp. 549-551.

3. Lanzillo, Fausto: Unusual Mechanism of Simultaneous Traumatic Rupture of Spleen and Stomach, Riforma med. **54**: 1029-1030 (July 2) 1938.

car. The child was riding in a toy express wagon at the time of the accident. Bystanders were unable to give exact details as to the method of injury, but from their rather scanty information, which was further verified by the physical examination, it seemed that the car wheel struck the left side of the child's abdomen and then glanced off without running over the body. According to the story of the parents, the child walked from the scene of the accident and experienced no immediate severe pains. A private physician stated that the patient had sustained only superficial bruises. About one hour after the injury the child became restless and cried considerably, holding his hand over the left upper quadrant of the abdomen. There was no history of nausea or vomiting prior to hospitalization.

The past history was of no importance except that the child had always been in the best of health. There was no history that might suggest previous attacks of malaria.

The child was fairly well nourished and well developed. He appeared to be rational and orientated but was in impending shock. He lay on the examining table on his right side with his knees drawn up and the palm of his left hand over the left upper abdominal quadrant. This posture was maintained throughout the preoperative period. His facial expression was apathetic, and at frequent intervals he whimpered with pain. The skin was moist and cold and had a rather characteristic greenish pallor. The admission temperature was 99.8 F. (rectal), the pulse rate 160, the respiratory rate 28 and the blood pressure 96 systolic, 40 diastolic.

Examination of the skeletal system revealed no evidence of fractures. The heart and lungs were normal, save for the rapid rate of the former. Over the lowest three ribs on the left side posteriorly from the midclavicular line were several superficial abrasions. There were similar abrasions over the left anterior-superior spine of the ilium and in the left lumbar region, but in none of these was the skin actually lacerated. The abdomen was splinted during respiration, and there was muscle guard over the entire left side of the abdomen. The point of maximum tenderness was in the left upper quadrant along the subcostal border. Questionable rebound tenderness was elicited over the right side opposite the umbilicus. The sign of Ballance was negative.[4] Auscultation of the abdomen revealed a "silent" intestinal tract. The patient vomited twice during examination, and no frank blood was seen in the vomitus. The blood count on admission showed 2,640,000 red cells and 24,650 white cells. Examination of the urine revealed no red cells or albumin and only a trace of sugar. A roentgenogram taken immediately on admission (sitting plate) and prior to the attack of vomiting failed to reveal evidence of free air under either leaflet of the diaphragm.

A diagnosis of a ruptured spleen with intra-abdominal hemorrhage was made, and the child was prepared for operation. There was some delay because the parents were reluctant to sign an operative permit, but during this time parenteral fluids were administered and blood donors were typed for transfusion.

Seven hours after the injury, with the patient under drop ether anesthesia, a laparotomy was performed; citrated blood was transfused during the operation. A left rectus muscle-retracting incision was made extending from the region of the xiphoid process almost down to the pubis, and when the peritoneum was opened considerable free blood was encountered. The blood, which contained several fairly large clots, was seen to be distributed throughout the peritoneal cavity, and approximately 500 cc. was aspirated during the operative procedure. Exploration of the left upper quadrant revealed the spleen to be ruptured completely with two entirely separated pieces, each attached at the pedicle. The two fragments were not equal in size, one being about two thirds and the other one third of the whole. The lacerated surfaces were irregular, shaggy and bleeding freely, though no arterial spurting was noted. The splenic segments were removed separately after suturing each pedicle with No. 1 chromic catgut. Further exploration revealed that the portion of the greater curvature of the stomach which normally lies in the splenic bed was ecchymotic and considerably traumatized. In the center of this traumatized area, which measured about 3 cm. in diameter, was a complete gastric perforation about 1 cm. in diameter which readily admitted the tip of a curved Kelly forceps. No gastric contents were spilled into the peritoneal cavity, and this was explained by the presence of a large blood clot over the site of perforation. A dulox suture was purse-stringed about the hole and the traumatized area was inverted.

Examination of the remaining abdominal viscera showed no further evidence of trauma other than a moderate degree of ecchymosis into the wall of the small intestine at the duodenojejunal flexure. The abdomen was closed in layers without drainage, with No. 1 chromic catgut single in a continuous suture to the fascial layers, four silkworm-gut stay sutures and clips to the skin.

The patient's postoperative course was stormy during the first forty-eight hours, owing in great part to bronchitis initiated most probably by the ether anesthesia. The highest temperature encountered was 103.8 F. (rectal) on the first day. Treatment during the first two days consisted of parenteral fluids (5 per cent dextrose in physiologic solution of sodium chloride), transfusions of citrated blood and sips of water by mouth. The postoperative blood counts on alternate days were red cells 3,980,000, white cells 7,600; red cells 3,750,000, white cells 8,900; red cells 3,900,000, white cells 9,000. The platelet count on the seventh postoperative day was 285,000. The Schilling differential count and the leukocytic morphology were normal. A soft diet was started on the third day; the skin clips were removed on the fifth day and the stay sutures on the ninth day. The abdominal wound healed by primary intention, and the child was discharged on the tenth day. When the child was examined three weeks later in the clinic the abdomen showed no incisional weakness and no areas of tenderness were present. The mother stated that the child was normal in every respect, had a healthy appetite and played in his usual boisterous manner. When last seen, four months after the date of injury, the child was in excellent health.

The pathologic examination was made by Dr. S. H. Gray. The gross specimen consisted of two pieces of spleen which together weighed 92 Gm. The specimen apparently had been forcibly torn apart. Both surfaces were irregular and craggy. The splenic capsule was smooth. On cross section the pulp was found to be firm and the trabecular system and malpighian corpuscles were seen to be prominent. Microscopically the capsule was thin and smooth. The germinal nodes were large, prominent and frequent. The splenic pulp was prominent, and only in several patchy areas was there any red pulp. No areas of old or recent infarction were seen.

COMMENT

Diagnosis in small children presents a problem which is due in great part to the lack of adequate mental intercourse between examiner and examinee. This case report proves to be an exception in that the history and physical features are almost classic in their clarity. A story of abdominal injury on the right followed by pain in the right upper quadrant, impending shock, leukocytosis and anemia can be taken almost word for word from any standard surgical textbook under the heading "Traumatic Rupture of the Spleen." Other injury could not be ruled out absolutely, and hence the x-ray study of the abdomen for possible free air under the diaphragm. The explanation of the lack of free intraperitoneal air in the presence of a gastric rupture lies in two factors: first the presence of a large blood clot in the gastric bed and second the failure of such a test to be exact, as is shown by the lack of such an observation in 30 per cent of proved gastric perforations.[5]

The problem further arises in this case as to the possibility of damage to the left kidney, for there were several abrasions in the left lumbar region. The absence of red blood cells in the urine and the anterior location of the tenderness helped the differential diagnosis.

Finally, the exact mechanism of injury to the stomach and spleen is a matter of interest. It would seem from the story

4. Graham, E. A.: Surgical Diagnosis, Philadelphia, W. B. Saunders Company, 1930, vol. 2, p. 725.

5. Petrén, Gustaf: Ueber den diagnostischen Wert des Röntgenologischen Nachweis freien Gases in der Bauchhöhle bei Ulcusperforation, Chirurg 9:259-266 (April 1) 1937.

as to the manner of injury, from the physical data and especially from the operative observations that the wheel of the automobile passed from the left iliac crest toward the xiphoid process and then the child must have been squeezed out, as it were, from under the tire. Thus the spleen and stomach were pinched between the wheel and the upper lumbar vertebrae.

SUMMARY

In a case of indirect traumatic rupture of the spleen there was a complicating gastric rupture. A splenectomy and gastric repair were performed with recovery of the patient.

This case presents the classic picture of a splenic rupture and emphasizes the importance of a complete and thorough examination of the entire peritoneal cavity in the face of intra-abdominal injury, for though the damage to the spleen explained all the symptoms and observations further exploration uncovered a gastric perforation.

FULMINATING CANCER OF THE PENIS

John K. Ormond, M.D., Detroit

The following instance of carcinoma of the penis is of interest for three reasons: (1) the long history and the nature of the precancerous lesion, (2) the fulminating character of the growth, and (3) the distribution of the metastases.

REPORT OF CASE

A man aged 62, married, machinist, the father of four children, stated that he had never had any venereal disease. Thirty-five years earlier, at the age of 27, he had been circumcised, and from that time forward on the scar of the circumcision, at the lower proximal rim of the sulcus, there was a dry crust continually forming, rubbing off and reforming.

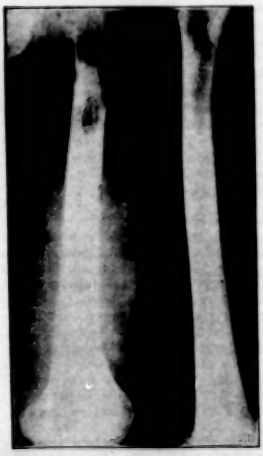

Fig. 1.—Appearance of the femurs.

Three weeks before his admission to the hospital this condition suddenly changed and a "sore" developed at the site of the crust and began rapidly eating away the end of the penis. At the same time a swelling appeared in the right groin, and he began having pain in the right hip extending down the anterior aspect of the thigh. About a week before admission the swelling in the groin ruptured and discharged serous and purulent fluid.

On admission his general physical examination showed nothing unusual except an old amputation of part of the left foot. The blood Wassermann reaction was negative. Involving most of the glans and a small portion of the shaft of the penis was a fungating ulceration, and in the right inguinal region was a yellowish mass the size of a golf ball topped by an irregular ulcer from which exuded a serous liquid. Biopsy showed squamous cell carcinoma, type I, of both penile tumor and inguinal mass.

On the fifth day after admission the distal half of the penis was amputated and the inguinal glands on both sides were excised. On the right the glands were found adherent to the femoral vein and were carefully dissected away, but a chain of large glands was found extending up under Poupart's ligament along the vessels. The inguinal wounds and penile wound healed, and even before healing was complete the patient was given high voltage roentgen treatment.

From the Division of Urology, Henry Ford Hospital.

Fig. 2.—Pelvis and upper part of right femur.

Thirty-two days after operation, while turning over in bed, he had severe pain in the upper part of the right thigh, and x-ray examination showed a destructive lesion in the femur with a pathologic fracture. A double hip spica was applied, which made him comfortable. He was sent home in the cast a month later and died at his home six weeks afterward.

A roentgenogram taken by his physician, Dr. L. E. Hamlin, of Norway, Mich., showed metastasis to the bones of the thorax. There was no local recurrence, either on the penis or in the inguinal regions, and it was striking how much the penis looked like a normal penis with the glans covered by a prepuce.

COMMENT

Stout, in his book on "Human Cancer," says: "On the whole the majority of the squamous cell epitheliomas of the penis are relatively benign, slow in their biological evolution. In spite of the fact that the patients often are not seen until the growth has been in existence for from eight months to a year, the majority of them have been successfully eradicated or destroyed. Metastases almost always go first to the inguinal glands. In rare cases, metastases have been reported in the liver, lungs, heart and stomach. Shivers reports a metastasis in the spine in one of his cases and Charannas and Simeon one in the fifth dorsal vertebra."

Fig. 3.—The chest shortly before death. Note the defect in the fifth rib.

In this case, the time from discovery of the tumor until death was only a little over four months, but the appearance of the tumor was preceded by a precancerous lesion of about thirty-five years' duration. A recurring crust on a circumcision scar is evidently nothing to be treated lightly.

BLACKWATER FEVER (HEMOGLOBINURIA) CAUSED BY SPIDER BITE

HENRY B. GOTTEN, M.D., MEMPHIS, TENN., AND
J. J. MACGOWAN, M.D., ASHLAND, MISS.

It is a common impression, particularly in this section of the country, that blackwater fever (massive hemoglobinuria) is caused only by malarial infections. It is known, however, that occasionally blackwater fever is caused by toxemia from drugs or by severe infections. Lesser grades of hemoglobinuria are common, especially since the use of the various sulfanilamide preparations has become universal. The term hemoglobimuria is used to designate the excretion of the blood pigment in the urine with the absence of red blood cells or with an insufficient number to account for the alteration of the urine. Blackwater fever is the term applied when the amount of this pigment is massive; this large quantity is sufficient to render the urine very dark or black in appearance.

Other causes of hemoglobinuria are organic and inorganic poisons such as quinine, phenol, glycerin and blood from incompatible donors, and severe toxemias due to burns and infections. Some cases of hemoglobinuria have been reported as being due to cold, and there are reports of cases in which the hemoglobinuria is paroxysmal in its occurrence.

We are reporting a case of blackwater fever caused by a spider bite. In a review of the recent literature we have been unable to find a similar case. Another interesting fact is that it is commonly thought that the "black widow" spider, Latrodectus mactans, is the only one which will cause a profound illness. In this instance the disease was caused by an insect not of the Latrodectus mactans variety but probably of the Amaurobius ferox species.

REPORT OF CASE

M. D. D., a girl aged 3 years whose family live in a rural community, was seen by one of us (J. J. M.) Aug. 12, 1939. August 11 the child was bitten on the left flank by a large brown spider. The mother, who removed the spider from the child's clothing, was certain that it was not of the "black widow" variety. At the time of the examination the child had a temperature of 102 F. and was vomiting frequently. There was a large, swollen, indurated area on the left side, just above the buttock, where the spider had punctured the skin. The child did not appear extremely ill, so that no medicine was prescribed, but general instructions were given to the mother. The following morning (August 13) the child passed black urine. On the receipt of this information she was immediately transferred to the hospital, arriving about 5 p. m. Her parents brought a specimen of urine. It was perfectly black, as if it were ink or as if there were charcoal in it. A specimen of the urine obtained on admission was examined spectroscopically by Dr. William B. Wendel, of the Department of Chemistry of the University of Tennessee. The pigment was identified as methemoglobin; it was present in concentrated amounts. It was acid in reaction and contained a large quantity of albumin, but there were no pus cells, red blood cells or other sediment in it. The specific gravity was 1.012.

The patient's temperature on admission was 102.2 F., the pulse rate was 130, and the respiratory rate was 22. On physical examination there was observed a large indurated area in the left flank about 8 cm. in diameter. In the center was a puncture wound of the skin, evidently where the spider had bitten her. Mild sedation and intravenous dextrose were administered at once, and blood was obtained for typing.

On laboratory examination the hemoglobin level was 59 per cent and the red blood cell count was 2,940,000. The white blood cell count was 17,800 with 91 per cent polymorphonuclears, 8 small lymphocytes and 1 large mononuclear. During the night the child seemed to be resting quietly and improving. The following morning she passed a quantity of urine the color of which had greatly improved. The vomiting had ceased, and she was able to take some fluids. About 3 o'clock in the afternoon, approximately seventy-two hours after the bite, the child suddenly went into shock and collapsed. Her temperature was elevated to 104 F., the pulse rate was 160 and the volume very poor, and the respiratory rate was 36. She was covered by a profuse perspiration and became cyanotic.

Within a very short time she was given 300 cc. of citrated blood, which was followed by 300 cc. of 10 per cent dextrose in distilled water. She responded quickly to the transfusion of blood and from that time on rapidly improved. The following morning her temperature was normal and it remained so for the duration of her hospital confinement.

The morning after the transfusion the hemoglobin estimation was 61 per cent and the red blood cell count was 3,410,000. The white blood cell count was 13,400 with 78 per cent polymorphonuclears, 17 per cent large lymphocytes, 1 large mononuclear and 4 eosinophils.

The last specimen of urine was clear in color, alkaline in reaction and free from sediment, pus or blood cells. The specific gravity was 1.002. The patient was kept under close observation the next week, during which time she showed no further effects from her illness. The urinary output was good, the temperature remained normal, and the swelling and tenderness at the site of the inoculation completely subsided. At last reports she had resumed her normal activities.

20 South Dunlap Street.

FATAL LEUKOPENIA FOLLOWING INTERNAL ADMINISTRATION OF CAUSALIN

OSCAR BERGHAUSEN, M.D., CINCINNATI

When aminopyrine is prescribed the physician should be on the alert for possible toxic symptoms, chiefly gastric in origin, for the patient may have an idiosyncrasy to the drug and leukopenia may be likely to develop if the use of the drug is continued. Unfortunately the physician sometimes does not recognize the aminopyrine content of a drug bearing a trade name, even though the label may bear the chemical nomenclature. Such a drug is on the market under the name of causalin,[1] which has been recommended for patients suffering from arthritis. Bernhard [2] tested its effects in 286 cases of arthritis but wisely recommended that its use be discontinued if gastric symptoms appear early in the treatment. He was able to administer a maximum dose of 60 grains (4 Gm.) daily with no signs of toxicity.

The following case is reported because death apparently was due to the continued use of a compound which contains approximately 1.82 grains (0.12 Gm.) of aminopyrine according to Bernhard.[2] Presumably he means the 7½ grain tablet or capsule of causalin. The question arises whether it would not be wise for all products containing aminopyrine to have the content of this drug written plainly on the label, for physicians are not familiar with the complex chemical nomenclature.

REPORT OF CASE

A married woman aged 52 was admitted to the Bethesda Hospital, in the service of Drs. G. E. Garwin and Spencer Hagen, Aug. 14, 1939, acutely ill with nausea and vomiting, no diarrhea and severe chills and fever. About a month before the onset of the present condition the patient's first physician had prescribed capsules marketed under the name of causalin. She had taken three capsules a day over a period of a month. She gave a history of arthritis which had developed twenty-five years previously, following the birth of a child and leading to permanent deformities of the extremities. There was nothing of further importance in the family history or personal history.

On admission to the hospital the patient was extremely toxic; the temperature was 102 F., the pulse rate 80 but irregular, and the respiratory rate 16. Three hours later the rectal temperature had reached 105.4 F., the pulse rate 80 and the respiratory rate 20. She was talking irrationally. Examination revealed ulcerations on the mucosa of the hard palate, with considerable edema and swelling of the pharynx making a laryngeal examination impossible. The ulcers were about 1 cm. in diameter with irregular margins and a white sloughing base. Acute gingivitis was present. Symptomatic medication included 1 liter of 10 per cent dextrose solution given intravenously, but to no avail.

1. Causalin is supplied by the Amfre Drug Company, New York, as 7½ grain (0.5 Gm.) tablets or capsules containing aminodimethylpyrazolon-quinoline sulfonate ethyl salicylate carbonate.

2. Bernhard, Robert: A Three Year Study of Arthritis, M. World 57:448-451 (July) 1939.

When seen in consultation thirty hours after admission to the hospital the patient was in a dying condition, with labored breathing and faint irregular pulse. The multiple ulcerations of the mucosa of the hard and soft palate were associated with marked edema. The tongue was furred and the breath foul. The thyroid and cervical glands were not enlarged. Edema of the lungs had developed with congestion at the base. The heart sounds were feeble and the pulse barely perceptible. Death occurred three hours later. Dr. Spencer Hagen reported that a vaginal examination revealed an enlarged uterus, with no demonstrable evidence of malignant growth. There was one ulcerative patch on the vulva. The spleen was not enlarged, and there was no jaundice or petechiae.

Of particular interest was the marked degree of leukopenia. On admission at 3 p. m. the red cells numbered 3,710,000 and the white cells 1,150 per cubic millimeter and the hemoglobin content was 64 per cent. The stained smear showed marked anisocytosis and poikilocytosis, and of 25 cells counted 23 were lymphocytes and 2 lymphoblasts. No polymorphonuclear or granular cells could be found. By 10 p. m. the white blood cells numbered 900 per cubic millimeter, by 11 a. m. the following morning 600 and at 3 p. m. 650. The patient died at 9 p. m. the day following admission; permission for autopsy was unfortunately refused.

The reddish bone marrow removed by sternal puncture showed about 4,500 white cells, all lymphocytes, an occasional lymphoblast, normally sized red cells and no normoblasts.

19 West Seventh Street.

AN UNFAMILIAR CAUSE OF LOSS OF WEIGHT

WILLIAM ALLEN PUSEY, M.D., CHICAGO

Early in 1937 I became conscious of the fact that I had almost lost my taste for food. The condition seemed to date from about the first of the year; I had been enjoying the flesh-pots over the holidays, and I assumed it was the result of that. But it continued and finally I concluded it was a permanent deterioration in my taste, for which, however, I had nothing to account. It was not a true loss of appetite because I would get hungry, but a loss of taste for food. It was so marked that I found it difficult to eat. In four months, by May, I had lost 20 pounds, from 185 to 165. A sudden unaccountable loss of 20 pounds in weight in an old man is a matter for concern, and I sought expert advice. I was thoroughly studied and nothing of importance was found, and particularly cancer in the abdomen was excluded.

Some time after that it gradually dawned on me that the deterioration in taste was the result of a dental plate which I had begun to wear just before the trouble developed. I had for some time worn a lower plate that carried five molar teeth, which never caused any disturbance of taste. The upper plate (the new one) proved to be the one that caused the trouble. It also carried five molars, three on one side and two on the other, connected by the usual vulcanite plate, which covered a good part of the hard palate.

The disturbance of taste could be directly associated with this upper plate. When it was left out the taste was normal; when put in, the taste was greatly impaired. I repeatedly, over weeks, controlled this fact. I could be eating a piece of beefsteak which had no more flavor than a ball of cotton, take the upper plate out, and the flavor would instantly become normal. This was so definite that I could prove it with a single mouthful. I could be eating a mouthful of steak which had no flavor, take out this upper plate, and the same mouthful of steak had its usual appetizing flavor. I made the most of my experiments with steak because with its delicate savor it was one of the best foods with which to experiment. In general, things of delicate savor showed the contrast most distinctly. Highly seasoned foods such as sausage or salads, and sweet foods, in both of which the taste was strong enough to overcome my defect, showed much less effect. Certain foods of odd flavor, such as kippered herring and sardines, became distasteful. If I took out my plate, even the same mouthful of either of them that had previously been distasteful regained its relish.

Thinking that the vulcanite might be a factor in the disturbance, my dentist made me a new plate of "vitallium"—a stainless metal—with the part connecting the teeth on the two sides somewhat narrower. But this made no appreciable difference. Finally he made me a cast upper plate of vitallium with a palatal bar one fourth inch wide. With this bar leaving most of the hard palate uncovered, the condition has been greatly improved. It has not been entirely relieved; food has still partly lost its relish, but not sufficiently to interfere greatly with eating, and I have regained my weight.

I think it is a common fact, not commonly recognized, that there is some diminution in taste caused by dentures, but that this should be so pronounced as to produce a loss of flesh that would suggest some serious disturbance of health is, I believe, quite unfamiliar. On this point I have consulted a considerable number of capable physicians of large experience—internists, surgeons and neurologists—to all of whom the fact was unknown. My dentist told me that he had not seen so distinct a case.

My original plate was made of a vulcanite composition. My subsequent plates were all made of vitallium. No facts came out while the case was being studied that suggested that the composition of the denture had anything to do with the case. It seemed to be purely a matter of the amount of the mouth that the denture covered.

It is easy to make a plausible surmise on the reason for the phenomenon, but I do not propose to consider that interesting subject in this communication. My sole purpose in recording this personal experience is to point out that a loss of weight sufficient to cause concern and obscure enough not to be discovered during months of search may be produced by a dental plate purely through the damage to taste which it produces and the subsequent loss of appetite.

7 West Madison Street.

Special Article

THE PHARMACOPEIA AND THE PHYSICIAN

THE MEDICINAL TREATMENT OF HYPERTENSION

HERMAN O. MOSENTHAL, M.D.
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NEW YORK

This is one of the second series of articles written by eminent authorities for the purpose of extending information concerning the official medicines. The twenty-four articles in this series have been planned and developed through the cooperation of the U. S. Pharmacopeial Committee of Revision and THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.—ED.

Thirty years ago hypertension was regarded as a compensatory phenomenon necessary for the maintenance of the circulatory functions at a normal pitch. Consequently no active interference with high blood pressure was seriously attempted. The realization of the importance of an elevated arterial pressure as a frequent, if not the most common, cause of premature death in persons of middle age has been a great stimulus to intensive studies of this subject. It is now known that a lowering of the blood pressure in instances of hypertensive states is compatible with unimpaired circulation and normal vitality. The means of treatment are three: medicinal, hygienic and surgical. Only the therapy with drugs is under consideration in this article.

THE VALUE OF MEDICINAL THERAPY

There is a widespread impression that the medicinal treatment of hypertension is absolutely valueless and that the patient with an elevated blood pressure should

be set adrift or, more recently, resort to surgery. It is extremely interesting to note that Ayman [1] in 1930, evaluating the therapeutic results in essential hypertension, arrived at conclusions that closely resemble present reports on the effects of operative procedures. Ayman writes:

> The successful treatment of essential hypertension by the use of many different drugs and methods of treatment has been reported at least two hundred times in the last decade. . . . In practically every article complete or partial symptomatic relief is reported. . . . In the majority of papers a moderate reduction in blood pressure is reported. Occasionally there is a marked reduction. . . . Marked symptomatic relief sometimes occurs without any reduction in blood pressure. Complete failure is seldom reported.

Ayman found that the symptoms of essential hypertension were definitely improved in 82 per cent of the cases by the serious and enthusiastic administration of diluted hydrochloric acid. All this means that suggestion and psychotherapy play an important part in the treatment of hypertension, though it does not gainsay that some medicaments may have an intrinsic merit of their own.

DRUGS THAT CAN LOWER BLOOD PRESSURE

The fact that blood pressure in some cases of hypertension can be reduced through vasodilatation or by depressing the central nervous system is well shown by the observations of Cady, Horton and Adson,[2] who used the following drugs to determine the response of hypertension and the suitability of the case for operation:

Sodium Nitrite.—Six doses of one-half grain (0.032 Gm.) each, given at half hour intervals, produces an effect in fifteen minutes, and its action is complete in from one to two hours. The nitrites lessen the tone of arterial muscle.

Amyl Nitrite.—This drug is given by inhalation; the effect manifests itself in fifteen seconds and lasts no longer than seven minutes.

Pentothal Sodium.—This is an anesthetic for intravenous use, in from 15 to 20 cc. of a 5 per cent aqueous solution, and is a progressive cerebral depressant.

Sodium Amytal.—Three grains (0.2 Gm.) administered by mouth and the dose repeated in from six to twelve hours acts as a depressant of the central nervous system; or 3 grains may be administered orally for three successive hourly periods.[3]

These drugs, in the doses indicated, are used as diagnostic measures for the determination of the fitness of a patient with hypertension for operation. The report of Cady, Horton and Adson demonstrates that vasodilators and sedatives can reduce blood pressure; however, the clinical application of such drugs for the prolonged control of hypertension has not been successful as a rule. This may be due to the fact either that these medications are not capable of accomplishing such a result or that physicians have not acquired the art of effective administration.

AIMS AND METHODS OF ADMINISTERING DRUGS FOR THE TREATMENT OF HYPERTENSION

The generally accepted explanation for an elevation of the blood pressure is an increase in the resistance to the arterial flow caused by a constriction of the arterioles at the distal part of the circulation. Whether this peripheral vasoconstriction is primary and is the reason for the hypertension, as is ordinarily assumed, or the peripheral vasoconstriction is a secondary, compensatory effect to hypertension, resulting from disturbed activity of the heart and musculature of the larger arteries, as a few of us believe, will make an enormous difference in the reasoning that governs the application of the so-called depressor drugs. At the present time the physician is decidedly handicapped because the functional pathology of hypertension is neither satisfactorily nor completely explained by any theory, and the conceptions, such as they are, can serve as working hypotheses but nothing more than that.

All drugs that depress blood pressure might in the strict sense of the term be classed as vasodilators, since they bring about dilatation of the arterioles. However, some medicaments relax the arterioles directly, and these may be regarded as the true vasodilators, while others cause vasodilatation by depressing the central nervous system, and finally there is a group of medicines that have been used empirically, which for want of a better name might be thought of as empiric remedies. Thus three groups of depressor drugs may be considered: (1) vasodilators, (2) sedatives, (3) empiric remedies.

The main object of the treatment of hypertensive states is to lower the blood pressure and maintain it at a level which will not result in the secondary changes that are often the cause of death when the blood pressure is persistently elevated. These complications must be accorded prophylactic as well as symptomatic therapy. They are mentioned here because they are part of the subject under consideration, though they have been or will be more thoroughly considered in other parts of this series of articles.

Cardiac dilatation, cardiac insufficiency, myocardial degeneration and coronary thrombosis are the heart conditions that are prone to occur. They should receive the same management whether hypertension exists or not, except that it is worth noting that cardiac dilatation in cases of hypertension is highly amenable to digitalis, since the heart muscle is often in excellent shape and responds exceedingly well.

"Cerebral accidents" may possibly be prevented by frequently repeated, moderate (from 200 to 300 cc.) venesections, which serve to keep the hemoglobin percentage and red blood cell count well within normal limits in patients with hypertension who are inclined to plethora.

Control of overweight should be insisted on to prevent cardiac insufficiency even if the lowering of the blood pressure by such means is not universally acknowledged.

The proper cathartics should be prescribed, so that gastrointestinal distention and straining at stool will be avoided.

Mild and prolonged exercise, without producing shortness of breath, will provide mental relaxation, maintain good physical health and should not result in cardiac dilatation when properly supervised.

A productive, sedentary routine occupation as a rule is more desirable for control of the central nervous system than permanent retirement, provided hypertensive encephalopathy does not exist and warp the acts and judgment of the patient.

The confidence of the hypertensive patient must be gained in full measure and he must learn to place full

1. Ayman, David: An Evaluation of Therapeutic Results in Essential Hypertension, J. A. M. A. **95**:246 (July 26) 1930.
2. Cady, J. B.; Horton, B. L., and Adson, A. W.: Drop in Blood Pressure Produced by Sodium Amytal, Sodium Nitrite, Amyl Nitrite and Pentothal Sodium: A Comparative Study, Proc. Staff Meet., Mayo Clin. **11**:823 (Dec. 23) 1936.
3. Allen, E. V., and Adson, A. W.: Physiologic Effects of Extensive Sympathectomy for Essential Hypertension: Further Observations, Ann. Int. Med. **11**:2131 (June) 1938.

responsibility on the physician; medicaments, as Ayman says, must be seriously and enthusiastically administered and should be varied frequently. Sometimes hypodermics are more useful than capsules. In part at least, this is confessedly psychotherapy for it has been learned that mental relaxation is of the greatest importance in lowering blood pressure.

SEDATION AND HYPNOSIS

While the other objectives of treatment of hypertension which have been mentioned are of equal importance to the nervous control of the patient, they should be regarded as an aid to the accomplishment of complete relaxation and satisfactory sleep. Tenseness during the active hours can often be avoided by sufficient rest, relief from excessive responsibilities, adjustment of the patient's personality and that of his family and friends, and some indulgence in pleasure. If these matters cannot be regulated so that a desirable effect on the blood pressure results, sedatives and hypnotics are in order. It is one of the basic principles of the treatment of hypertension that adequate rest should be obtained. Rest in the prone position for a half to one hour will usually be followed by a considerable drop in blood pressure, and such lowering of the arterial tension will often be maintained for some time subsequently. The heart and the arteries are relieved from the strain of the hypertension during this interval. Serviceable directions are:

1. Two hours' rest after lunch, flat in bed or on a couch, without interruption by friends or by the telephone.
2. Eight hours in bed at night.
3. The remainder of the day indulgence in usual activities and exercise, but avoidance of any exertion that will cause shortness of breath.

If adequate rest is not obtained, sedatives and hypnotics are indicated.

Previous to the intensive development of the barbital compounds, that is up to about 1930, the bromides and chloral were used extensively, and they are still employed by many.

Bromides: *Ammonium, Potassium and Sodium Bromide.*—Sedative dose: 0.3 to 1 Gm. (5 to 15 grains) repeated every four hours. Hypnotic dose: 2 Gm. (30 grains). The bromides may be used singly or in combination; they are hygroscopic and should not be prescribed in powder form or capsules; there are a number of ready made tablets that are acceptable; the effervescent preparations are not advisable in cases of hypertension, as they distend the stomach and tend to embarrass the heart; the bromides should be taken in solution and well diluted with water.

Chloral Hydrate.—Sedative dose: 0.2 to 0.7 Gm. (3 to 10 grains) repeated every four hours. Hypnotic dose: 0.7 to 2 Gm. (10 to 30 grains). The drug deteriorates on standing and hence cannot be dispensed in powders, capsules or tablets; it has an acrid taste which has never been successfully disguised; it is customarily prescribed in solution with elixir of lactopeptin and taken well diluted with water or orange juice. When necessary, it can be effectively administered in starch paste by rectum. The individual susceptibility to chloral varies enormously. I have seen one patient —a 200 pound (90 Kg.) man, broad shouldered and well over 6 feet (183 cm.) tall—who had trouble keeping awake during the day with a 5 grain (0.33 Gm.) dose, while a small woman scarcely obtained a night's sleep after taking 30 grains (2 Gm.). At times chloral produces restlessness and may even result in a condition that is little short of delirium; it occasionally causes eczema.[4] I have never seen any serious toxic effects from chloral hydrate and some of the older physicians at Bellevue Hospital, where the drug used to be administered liberally and frequently, tell me that they have witnessed no harm from it, though Grabfield[5] says "There is no doubt that in toxic doses it kills by its effect on the heart, but the fear of this side action has been engendered by the large dosage that has always been recommended up to the last five years."

Elixirs of Barbital and Barbital Compounds

	One Fluidrachm Contains	Hypnotic Dose
Elixir of phenobarbital, N. F.	0.015 Gm. (¼ grain)	0.1 Gm. (1½ grains)
Elixir alurate	0.03 Gm. (½ grain)	0.065 Gm. (1 grain)
Elixir amytal	0.015 Gm. (¼ grain)	0.1 Gm. (1½ grains)
Elixir Dial	0.05 Gm. (¾ grain)	0.1 Gm. (1½ grains)
Elixir barbital, N. F.	0.12 Gm. (2 grains)	0.3 Gm. (5 grains)
Evipal—oxidized in the body		0.25 Gm. (4 grains)
Seconal—oxidized in the body		0.1 Gm. (1½ grains)

Barbital and Barbital Compounds.—Many of these have been successfully evolved during the last decade, so that at the moment there are more of them available than can be utilized. They are as a rule given as tablets or capsules; the sodium compounds are soluble but many of them deteriorate in solution and it is probably the best plan to resort to the prepared elixirs such as those in the National Formulary, in the comparatively rare instances when liquid medication is indicated.

The available elixirs of barbital and barbital compounds are listed in the accompanying table.

In the treatment of hypertensive patients the main objective is to avoid nerve tension and strain during the day and make certain of satisfactory sleep at night; such conditions may exist naturally; if they do not, they must be provided for by medication. The barbiturates are at present believed the best means to accomplish this. In order to prevent a cumulative effect they may at times be alternated with the bromides or chloral.

Barbital and barbital compounds vary in potency; hence the dose of each is different from the others. They are administered with the object of producing sedation, hypnosis or anesthesia. In the treatment of hypertension, sedation during the day and hypnosis at night are ordinarily the main objectives, so that the dosage of the barbiturates will differ during the day and at night. The susceptibility of patients varies a great deal, so that the dose has to be adjusted to the individual response. Some of the barbiturates act rapidly and for a comparatively brief period, while others have a somewhat delayed effect and carry through much longer. Many of the barbiturates are oxidized in the body, while others are eliminated in the urine; it is obvious that the latter may result in a cumulative effect and should be given intermittently, while this precaution, theoretically at least, is unnecessary for the drugs that are destroyed by the body tissues. Although all the barbiturates depress the central nervous system, there are some that affect the motor system more than others and hence are especially useful in controlling the tendency to convulsive seizures or actual convulsions.

4. Baer, R. L., and Sulzberger, M. B.: Eczematous Dermatitis Due to Chloral Hydrate, J. Allergy **9**: 519 (July) 1938.
5. Grabfield, G. P.: The Use of Hypnotics, J. A. M. A. **107**: 1381 (Oct. 24) 1936.

Many barbital compounds are offered that have been developed at the expense of an enormous amount of time and effort. It is a great pity that plain, carefully gathered, comparative data are not available for these drugs; it would aid the practitioner a great deal in their intelligent administration. The following list has been prepared; it is necessarily only a partial one.

BARBITAL AND ITS COMPOUNDS FOR SEDATION AND HYPNOSIS

For sedation the dose is from one sixth to one fourth the hypnotic dose and is given at intervals during the day; phenobarbital, a long acting barbiturate, has been the most used of these drugs for sedation.

For hypnosis the short acting barbiturates should be employed to combat delayed or intermittent sleep; the long acting barbiturates for complete, constant wakefulness; at times a combination of a short and a long acting barbiturate is effective.

The response to barbiturates is variable, and sedative and hypnotic doses have to be determined by trial and error in each individual.

Some of these drugs are cumulative, as they are not destroyed in the body, and hence they should be used intermittently.

Although all the barbiturates depress the central nervous system, there are some that affect the motor system more than others and hence are especially useful in the handling of the tendency to convulsive seizures or actual convulsions (phenobarbital and amytal and their sodium salts in the subsequent list).

The drugs to be mentioned are supposed to be given in capsule or tablet form. When it is desired to use fluid medication one should resort to the prepared elixirs, as most of the barbiturates that are soluble deteriorate in solution.

In each group the drugs are arranged according to duration of effect; the shortest acting ones are put first.

SOME OF THE BARBITAL PREPARATIONS AND THEIR ACTION

Action rapid, of comparatively short duration (from eight to twelve hours):

Pentobarbital sodium (N. N. R.), oxidized in the body. Hypnotic dose 0.1 Gm. (1½ grains).

Ortal sodium (N. N. R.), oxidized in the body. Hypnotic dose 0.3 Gm. (5 grains).

Action medium duration (twenty hours more or less):

Amytal (N. N. R.), oxidized in the body. Hypnotic dose 0.1 Gm. (1½ grains).

Amytal sodium (N. N. R.), oxidized in the body. Hypnotic dose 0.2 Gm. (3 grains).

Phanodorn (N. N. R.), mostly oxidized in the body, only small amounts appearing in the urine. Hypnotic dose 0.2 Gm. (3 grains).

Neonal (N. N. R.), oxidized in the body. Hypnotic dose 0.1 Gm. (1½ grains).

Alurate (N. N. R.), over 80 per cent oxidized in the body, the remainder eliminated in the urine in less than twenty-four hours. Hypnotic dose 0.065 Gm. (1 grain).

Long acting (more than twenty hours):

Barbital (U. S. P.), excreted in the urine, partly oxidized in the body. Hypnotic dose 0.3 Gm. (5 grains).

Soluble barbital (barbital sodium) U. S. P., excreted in the urine, partly oxidized in the body. Hypnotic dose 0.3 Gm. (5 grains).

Ipral calcium (N. N. R.): "It is claimed that it is excreted rapidly, but some action commonly persists for twenty-four hours" (N. N. R., 1939, p. 115). Hypnotic dose 0.12 Gm. (2 grains).

Phenobarbital (U. S. P.), excreted in the urine, partly oxidized in the body but to a greater extent than barbital. Hypnotic dose 0.1 Gm. (1½ grains).

Soluble phenobarbital (phenobarbital sodium) U. S. P., excreted in the urine, partly oxidized in the body but to a greater extent than barbital. Hynotic dose 0.1 Gm. (1½ grains).

VASODILATORS

Vasodilators should be the ideal means of controlling hypertensive disease if it is true, as generally accepted, that the cause of an elevated blood pressure resides in a primary peripheral constriction of the arterioles. The fact that these preparations either are inert in small doses or produce disagreeable sensations and even vasomotor collapse when administered in therapeutically effective amounts would point away from spasm of the arteriolar musculature as the process responsible for arterial hypertension. Certain of the vasodilators (glyceryl trinitrate under the tongue, amyl nitrite by inhalation) are invaluable in the treatment of angina pectoris because they result in prompt dilatation of the coronary vessels. When the dosage is sufficient to bring about a general reduction of arterial and arteriolar tone and a lowering of the blood pressure, vasomotor collapse often follows. Recently Lueth and Hanks[6] have demonstrated this for glyceryl trinitrate; they accentuate the fact that the resulting vasomotor collapse depends as much on the susceptibility of the patient as on the size of the dose. The so-called vasodilators that are in common use and their dosage are as follows:

Amyl Nitrite.—This is administered by inhalation; it has a vasodilator effect in from ten to fifteen seconds and its action is terminated within seven minutes. Average dose: 0.2 cc. (3 minims) dispensed in glass pearls, which are crushed beneath the nostrils and inhaled.

Glyceryl Trinitrate (nitroglycerin).—Vasodilator action starts within a minute and lasts about half an hour; this is the effect when the drug is swallowed; when it is placed under the tongue the results are more rapid and fleeting.

Spirit of Glyceryl Trinitrate (spirit of nitroglycerin) U. S. P.—The average dose is 0.06 cc. (1 minim).

Tablets of Glyceryl Trinitrate (tablets of nitroglycerin) U. S. P.—The average dose is 0.0006 Gm. (1/100 grain).

Sodium Nitrite (U. S. P.).—This is a white powder that deliquesces in the air and hence is dispensed in solution. It produces a vasodilator effect in fifteen minutes which is complete in from one to two hours. Average dose: 0.06 Gm. (1 grain).

Erythrityl Tetranitrate (erythrol tetranitrate).—The vasodilator action begins in fifteen minutes and persists for three or four hours.[7] Pure erythrityl tetranitrate is a crystalline mass which explodes on percussion; hence it is marketed chiefly in the form of tablets.

Diluted Erythrityl Tetranitrate (diluted erythrol tetranitrate) U. S. P.—This preparation is about 50 per cent erythrityl tetranitrate and 50 per cent lactose. Average dose from 0.03 to 0.06 Gm. (one-half to 1 grain).

Bismuth Subnitrate.—Stieglitz[8] advanced the ingenious idea that in the intestinal tract through bacterial action nitrites are slowly liberated from bismuth subnitrate and that the blood pressure would be lowered thereby. The bismuth subnitrate was administered in 10 grain (0.65 Gm.) capsules three times a day. Stieglitz obtained excellent results with this therapy while others have been unable to duplicate them. Stieglitz

6. Lueth, H. C., and Hanks, T. G.: Unusual Reaction of Patients with Hypertension to Glyceryl Trinitrate, Arch. Int. Med. 62:97 (July) 1938.
7. New and Nonofficial Remedies, Chicago, American Medical Association, 1939, p. 337.
8. Stieglitz, E. J.: Arterial Hypertension, New York, Paul B. Hoeber, Inc., 1930.

advocated the use of the bismuth subnitrate over a period of many weeks, and it may be that lack of sufficiently long administration accounts for the failure to obtain the same effects.

EMPIRIC REMEDIES

Empiric remedies, in a sense, are vasodilators if they lower blood pressure; on the other hand, their mode of action is largely unknown, and it is doubtful whether any of them act specifically in relaxing the musculature of the arterioles. Consequently they cannot be regarded as true direct vasodilators. Thus far no drug or preparation merits the designation specific remedy for hypertension, though many of them are spoken of in that way by their sponsors.

Thiocyanates.—Sodium or potassium thiocyanate 0.2 Gm. (3 grains) to 0.3 Gm. (5 grains) in solution three times a day has been widely used in the treatment of hypertension. This drug is also available in the National Formulary as an elixir containing 0.16 Gm. (2½ grains) per teaspoonful.

A recent and careful study[9] offers substantial evidence that thiocyanates may lower blood pressure appreciably in cases of hypertension and relieve the symptoms.

Toxic effects from thiocyanates have been reported frequently; extensive toxic dermatoses have been described. Goldring and Chasis[10] reported two deaths resulting from poisoning during thiocyanate therapy. (Earliest symptoms: muscular weakness and nausea followed by vomiting, mental confusion, delirium, convulsions, coma, death.)

Barker[11] found that "the reduction of blood pressure and the relief of symptoms obtained . . . corresponded to the level of cyanates in the blood. The optimum therapeutic level would seem to range between 8 and 12 mg. per hundred cubic centimeters, and significant toxicity begins to appear at from 15 to 30 mg. The individual tolerance varies greatly, the different levels being obtained with widely varying doses. The cyanates may reach hazardous concentrations . . . in some individuals, so that the administration of the thiocyanates is believed to be dangerous unless controlled by close observation and blood cyanate determinations."

Robinson and O'Hare,[9] following Barker's[11] lead of controlling the situation by analyzing the blood for cyanates, found that a level of from 7 to 12 mg. per hundred cubic centimeters was the optimal blood cyanate concentration and that great care should be taken with blood levels above 12 mg. per hundred cubic centimeters. In seventy-five cases average drops of 40 mm. systolic and 20 mm. diastolic occurred in 63 per cent; hypertensive headaches were relieved in eighteen of twenty cases. Toxic symptoms occurred in twenty-nine cases, or 38 per cent. The less serious toxic complications, accounting for twenty-three of these twenty-nine cases, consisted of nausea, weakness, dermatitis, purpura and a decrease in libido. Serious complications consisting of dermatitis exfoliativa, congestive heart failure, cerebral thrombosis, angina pectoris and psychoses occurred in six cases.

There is no doubt that the thiocyanates in sufficient doses will lower blood pressure and relieve the symptoms of hypertension, though their administration is associated with considerable danger. Nichols[12] some time ago, recognizing these possibilities, suggested that thiocyanates be given intermittently, during a week or two each month, and that a course of treatment should be instituted whenever the blood pressure rises. Control of the thiocyanate administration by quantitative determination of the cyanates in the blood, as suggested by Barker, is a distinct advance in this therapy. The original conclusion of Barker that the optimal therapeutic level ranges between 7 and 12 mg. per hundred cubic centimeters of blood and that higher concentrations may be associated with toxic manifestations has been verified and furnishes an excellent guide to the rational use of the cyanates.

Davis and Barker[12a] found, in a small group of patients who were resistant to thiocyanate therapy, that section of the splanchnic nerves, in some unknown manner, increased the sensitivity to the thiocyanates and made them effective in reducing blood pressure.

Iodide.—Small doses of potassium or sodium iodide, from 0.065 to 0.3 Gm. (1 to 5 grains), will sometimes prove to be effective remedies for hypertension. Why they are of value in the occasional case and not in all cases is not clear. This dose of the iodides should be given in solution, well diluted, once a day. Large or progressively increasing amounts of the iodides as they are administered for syphilis do not accomplish anything in essential hypertension. Tablets are available of organic iodine compounds such as calcium iodobehenate, U. S. P. (sajodin), or lipoiodine-Ciba, and one or two of these tablets a day may be more convenient for the patient than the fluid medication. Iodide has been marketed in various combinations with the barbiturates, calcium and theobromine for the treatment of hypertension; such prescriptions may be devised according to the judgment of the individual physician.

Miscellaneous Remedies.—Tissue extracts taken from the pancreas, liver, muscle and elsewhere have been used and endorsed; after prolonged and intensive trial thus far none of them have proved satisfactory in the treatment of hypertension.

Histamine, acetylcholine, acetyl-beta-methylcholine according to Weiss[13] are either unsuitable or ineffective for the treatment of persistent hypertension.

Internal secretions have not been successfully applied in the treatment of hypertension; this does not gainsay that they should not be prescribed when they are indicated for various conditions that may coexist with hypertension. It is interesting and worthy of note that the idea that hyperadrenalism is responsible for hypertensive states is losing ground.[14]

Watermelon seed and mistletoe have yielded various preparations that have been accredited with the properties of lowering blood pressure; however, they have not received general endorsement.

SUMMARY

Since there are no means by which an elevated blood pressure can be appreciably and consistently lowered, the medical treatment of hypertension has resolved itself into the establishment of the most perfect possible physical and mental control of the patient; in this therapeutic scheme drugs are important for the achievement of the utmost results.

889 Lexington Avenue.

9. Robinson, R. W., and O'Hare, J. P.: Further Experiences with Potassium Thiocyanate Therapy in Hypertension, New England J. Med. **221**:964 (Dec. 21) 1939.
10. Goldring, William, and Chasis, Herbert: Thiocyanate Therapy in Hypertension, Arch. Int. Med. **49**:321 (Feb.) 1932.
11. Barker, M. H.: The Blood Cyanates in the Treatment of Hypertension, J. A. M. A. **106**:762 (March 7) 1936.
12. Nichols, J. B.: The Pharmacologic and Therapeutic Properties of the Sulfocyanates, Am. J. M. Sc. **170**:735 (Nov.) 1925.
12a. Davis, L., and Barker, M. H.: Clinical and Experimental Experiences in Surgical Treatment of Hypertension, Ann. Surg. **110**:1016 (Dec.) 1939.
13. Weiss, Soma: Recent Advances in the Treatment of Arterial Hypertension, M. Clin. North America **19**:1343 (March) 1936.
14. Rogoff, J. M., and Marcus, Emanuel: Supposed Role of the Adrenals in Hypertension, J. A. M. A. **110**:2127 (June 25) 1938.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE. HOWARD A. CARTER, Secretary.

SHOES AND FEET

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In this discussion of the foot problem I propose to divide the subject into two parts:

1. The problem of the symptomless foot.
2. The problem of the painful foot.

This division would seem logical, since the painless foot may at any time become an exquisitely painful one. Therefore, proper shoeing of such a foot must necessarily be prophylactic. It will be shown in the following discussion that shoes can be made and properly fitted to a normal foot.

THE SYMPTOMLESS FOOT

It is practically impossible to define a normal foot, since it is obvious that no two feet are exactly alike even in the same individual. There are, however, some things common to all so-called normal feet: the number of bones, articulations, ligaments, fasciae, bursae, tendons, muscles, nerves and circulatory apparatus. All these structures conform more or less to a regular pattern in their relations to one another.

A normal foot may be defined as one that exhibits through its life history no subjective or objective symptom or pathologic condition. A so-called normal foot, however, may become a painful or abnormal one under certain conditions. A foot that shows physical abnormalities may be perfectly normal from the point of view of function and painlessness.

The normal foot, then, shows certain definite physical aspects which are common to all feet, but these feet vary in size, shape and contour both in the non-weight bearing and in the weight bearing position. Such a foot, when subjected to bad shoeing, bad weight bearing surfaces or overweight, may gradually or suddenly become painful. Normal feet may become abnormal as the result of illness, sedentary occupations or bad posture. A foot that is normal in the country where the individual lives on the ground may be a very painful one when suddenly required to carry the owner about on city pavements. In the days of the horse it was learned that when the horse's feet and legs began to give out on paved city streets they would recover if the horse was sent to the country and placed in a soft pasture.

It has been stated by many writers that the foot should be shod in such a manner as to imitate the foot of the savage in his native habitat. The answer to this is that when the savage visits the city his feet will not stand up under the vicissitudes of pavements and hard floors. Civilization requires that those who live in civilized communities must wear shoes. The individual requires from the shoe shop shoes that look well and that conform to the style of the day. The sensitive and fastidious person resents anything that makes him abnormally conspicuous. Shoes that look and seem freakish are not well tolerated by these individuals. Therefore the so-called corrective, anatomic and orthopedic shoes are not well accepted by the majority of persons.

It is possible also that a normal foot without symptoms of any trouble may become a painful foot in such shoes because they do not fit the individual foot in every particular. Buying a pair of shoes is much like buying a hard hat. If the hat does not conform to the irregularities of the skull it may be very uncomfortable. One must therefore try on several hats to find one that is comfortable. The hat situation is different from the shoe situation only in that the weight of the body is on and in the shoe.

SHOE PROBLEMS

Shoes in this country are constructed on standard lasts, and it is here that trouble begins. Feet do not conform to these standard lasts even though there are variations in sizes and shapes of shoes. It is well known that two pairs of shoes made on the same last will not feel the same on a pair of feet. This is due to differences even in the same material and also to the fact that wet leather, wetting the last, does not draw on the last in exactly the same manner, so that the second pair will not be a duplicate of the first pair.

There are no two feet exactly alike even of the same individual. Thus the problem of properly fitted shoes is an individual one for each foot. Since more than 400,000,000 pairs of shoes are manufactured in this country yearly it would seem unwise to embark on an ideal program that would meet the needs of individuals: the economics of the present shoe situation would be ruined and the cost of shoes would be prohibitive both for the manufacturer and for the consumer. This does not mean that the situation cannot be improved. There is no doubt that something can be done to improve materially conditions as they now exist without extra cost to the manufacturer or to the consumer.

The requirements for a satisfactory shoe to be used on a symptomless foot are:

1. Length.
2. (*a*) Width of sole and height over toes.
   (*b*) Width of heel.
3. Height over instep.
4. Line of shoe.
5. Height of heel.
6. Shank of shoe.

1. *Length.*—The shoe must be of sufficient length so that the end of the great toe is not against the toe end of the shoe. (*a*) Variations in length must provide for the increase in the length of the foot of those who carry heavy loads. (*b*) The shoe must not be so long that the foot slides forward from the heel upper of the shoe.

2. *Width.*—The front of the shoe, for example the vamp, should be wide enough so as not to compress unduly the toes at the sides or on top. This part of the shoe, however, must be snug so that the leather will not wrinkle. If the width of this end of the shoe is too great the forefoot will slide about and corns and calluses will form. A similar condition will result if the vamp is too tight; also the action of the toes will be cramped.

A fault altogether too common in ready made shoes is that the heel inside the shoe is too wide. This fault allows the foot to slide laterally and the heel to slip up and down with each step. The heel should be held snugly both at the sides and behind. It ought to be a part of the manufacturer's job to pay as much attention to heel widths as to sole widths.

3. *Height Over Instep.*—There is not room enough in the average shoe over the instep, especially for the medium to highly arched foot. When shoes are put on such a foot they are laced so snugly that the instep is pushed downward, thus mechanically elongating the foot and stretching the arch so that in time symptoms of foot strain may develop.

4. *Line of Shoe.*—The line of the shoe must correspond to the lines of the sole of the foot. No attempt should be made to have the shoe thrust its lines laterally against the lines of the sole either outwardly or inwardly. To do so will unduly compress the side of the foot and cause irritation and corns. This is especially true in cases in which there is a circulatory disturbance of the feet or diabetes.

5. *Height of Heel.*—Attempts have been made to have bills passed in the state legislatures to regulate the height of heels. It would be just as sensible for these bodies to legislate standard eyeglasses for eye troubles. The height of the heel should depend on the loss of passive dorsal flexion of the foot and should be tested as follows:

The subject is seated with his ankle resting on the examiner's hand; the knee is completely extended; the leg level and all the muscles in that extremity are completely relaxed. The examiner adducts the foot very slightly and gently passively dorsiflexes the foot until it will go no further under gentle manipulation. He then estimates or measures the loss of dorsal flexion, if any, by measuring the distance between the sole of the heel and a plumb line falling from the great toe joint. This distance will give the height of heel necessary for that individual. Any heel lower than this may cause pronation of the foot, spreading of the forefoot and pain and cramps in the calf of the leg and also cause callosities to form under the ball of the foot. It may even cause symptoms of knee and back strain.

The highly arched foot, by and large, is apt to be associated with a short heel cord. When a person with this type of foot stands it will be seen that pronation and lateral squatting of the feet occur and must occur if the person is to get his heels on the ground. When such a person is asked to rise on tiptoe it will be seen at once that the pronation disappears. Persons with this type of foot are usually fast walkers and love agile games and dancing. They dislike to stand about and if required to do so for any length of time find themselves leaning against or resting on some support. When long standing is required, general fatigue is apt to ensue.

6. *Shank of the Shoe.*—Probably less intelligent attention is paid to the shank of the shoe than to any other portion. From an engineering point of view the shank fit is most important. It has been stated by many that a support under the arch splints the muscles of the sole and causes muscle atrophy. If this is so, then why not discuss atrophy from shoe pressure on other parts of the foot? A steel beam, designed to carry a constant load, will carry twice as much weight if that weight is distributed over the length of the beam and is not concentrated in the center. This is more or less true of the foot except that the load is on the ends of the beam. If the whole sole of the foot is made a weight bearing surface, without undue pressure under the arch, it will be mechanically easier to carry the distributed load. It seems reasonable to suppose then that this principle applied to a shoe would at least minimize fatigue and improve the efficiency of the individual. To meet this situation in the shoe, the shank must fit the individual foot; and since there are many variations in the height of arches, it is necessary to have the shank so constructed that it will fit each individual foot. This can be done. In most shoes there is a steel shank placed between the soles. This shank in general is always the same with the exception that some manufacturers have the shank a little higher or a little lower than others. Such shanks are usually so constructed that they break if one attempts to bend them. It is impossible, therefore, to fit this type of shank to the arch of the foot.

A solution is to construct a last a little higher than the present standard last and then to construct a shank which can be raised or lowered, which will not break when bent or when under a load, and which will stay put once it is fitted up to the arch by being bent up or down as occasion requires. Such a shank can be built.

The stiff, hard shank is breakable and cannot be adjusted and its only merit is that it prevents the shank of the shoe from becoming flattened out. It does help to keep the shape of the shoe as age creeps on it.

The shoe without a shank, or the plastic type, is easily bent and sags under a load. It allows the front of the sole and the toes to turn upward, which makes the top of the shoe pull the instep downward. These shoes are supposed to imitate the mocassin of the savage who lives on mother earth but not on concrete.

Schwartz[1] with his basograph has shown that the normal person walks in this manner: The heel strikes the ground first, then in moving the body forward to complete the step the outer border of the foot is in contact with the ground, especially the fifth metatarsal, at which point most of the body weight is borne. Next the great toe joint and the great toe strike the ground, propelling the body forward by a tremendous thrust toward the next step by the opposite leg. If the shank of the shoe fits up gently under the sole of the foot, the foot in the second and third positions has enough additional even distribution of its weight bearing surface on the sole to relieve the strain on the fifth metatarsal body and head and under the great toe. In the standing position, which is harder on feet than any other, the snugly fitted shank relieves the three contact points of the foot of some of the weight which they are called on to support in the average shoe as at present constructed.

Shoes built on the scheme as outlined should not be considered as corrective, orthopedic or anatomic. They should be regulation shoes for all who must wear shoes. They may be considered to be preventive shoes. The shoe clerk must be taught how to fit the shanks as well as other points of the shoe. There should be as much attention paid to teaching the fitting of this part of the shoe as there is to any other part. However, the shoe clerk must not get the idea that in fitting these shoes he is going to relieve all foot ailments. He is already doing that very thing with the so-called corrective shoes, but, unfortunately for the public, he does not know just exactly what he is doing. People with abnormal foot conditions should consult their physicians; if the physician cannot help his patients he should refer them to the consultant in whom he has confidence.

A shoe constructed on the lines laid down will not cost the manufacturer any more than does the shoe he is now making. Therefore, the serious objection of

1. Schwartz, Plato; Heath, Arthur; Misiek, William, and Wright, John: Kinetics of Human Gait, J. Bone & Joint Surg. 16:343-350 (April) 1934.

cost to the manufacturer and wearer is nil. It should be possible for all manufacturers to plan and make shoes on the principles described so that all may be treated without discrimination.

THE PAINFUL FOOT

The problem of the relief of patients whose feet are giving them trouble cannot be solved by a single universal remedy, i. e. the orthopedic shoe. In the first place there are too many different kinds of painful feet and in the second place no two feet are alike. It would seem, then, that the present orthopedic shoe is designed so that the foot must fit the shoe instead of the shoe fit the foot. When those members of the medical profession who are interested in foot troubles and the manufacturers of shoes realize this fundamental principle and get together on it, a solution of part of the problem may be reached.

Each patient with symptoms of pain in his feet is an individual whose anatomic, physiologic and pathologic condition is not exactly the same in all details as his neighbor, even though he may be suffering from the same complaint. A review of some of the causes of painful feet will convince almost any one that a standardized orthopedic shoe cannot possibly be the answer.

Pain in the feet may be due to bad mechanics or to disease.

Under bad mechanics can be listed ill fitting shoes, sedentary life, sudden change of weight bearing surfaces from soft to hard, change of occupation, overweight, fatigue, carrying heavy loads when it has not been done before, congenitally weak feet, relaxed feet in which there is increased mobility especially in the pronated and abducted positions, weakness due to debilitating diseases, and bad union of fractures in the legs and feet.

Under diseases may be included circulatory disturbances (intermittent claudication, Buerger's disease, varicose veins), diabetes, arteriosclerosis, Sudeck's atrophy, arthritis, gout, rigid valgus from peroneal spasm, diseases and injuries involving the peripheral nervous system, e. g. poliomyelitis and spastic paralysis.

When a patient is seen who complains of pain in the arches, feet, ankles, toes, calves of the legs, knees and thighs and sometimes a lame back, one should not be too ready to accept a diagnosis of "broken arches." A thorough examination of the feet should be made to see whether the trouble is due to foot strain, but further examination is necessary to find out whether or not there is some underlying constitutional or circulatory difficulty present which may account for the symptoms.

SYMPTOMS

Pain is the predominating symptom of foot strain and may occur in the toes, in the ball of the foot, under the arch in the plantar structures, through the instep (especially on the medial aspect), about the internal malleolus and, if pronation is present, about the external malleolus, under the os calcis, in the calf of the leg, along the shin bone, in the knee under the patella or patellar tendon, about the internal condyle, in the thigh muscles and in the low part of the back, either the sacral or the lumbosacral region. These symptoms may occur singly or there may be combinations of locality; e. g. a patient may have backache without pain elsewhere in the lower extremities. Cramps may be complained of in the toes, soles of the feet or any of the leg muscles, especially the calf. The "growing pains" of children are nearly always due to foot strain and not to "rheumatism."

EXAMINATION

The foot should be examined in two positions—weight bearing and at rest. In the weight bearing position one should note the relation of the feet to the knees. Does the forefoot spread? Are there deformities of the toes when the patient is standing which are present or absent when he is sitting? Does the whole forefoot abduct? Does the foot pronate? Does it abduct and pronate? Do or do not the pronation and abduction disappear when the patient is asked to stand on tiptoe?

The whole diagnosis of the condition should not be made from the weight bearing position. Many a patient has been turned down for military or other service because a diagnosis of flatfoot has been made with the patient standing barefoot. This is all wrong and should be fought vigorously. A person under general physical examination who has this type of foot on weight bearing is usually perfectly normal in the ordinary well built shoe which meets the specifications of shoes for normal feet.

In examining the foot at rest the examiner looks for signs of abuse, such as corns on the toes, calluses under the ball of the foot or on the inner aspect of the great toe or over the lateral aspect of the head of the fifth metatarsal, bunions, hallux valgus, valgus minimi digiti, cock up toes, hammer toes, depression of the heads of the second, third and fourth metatarsals, prominent scaphoids, exostoses especially on the dorsum of the foot, hallux rigidus, swelling about the ankle joint, over the dorsum or under the sole of the foot, thickening of the os calcis, especially about the insertion of the achilles tendon, wind puffs about the malleoli, thickening of the achilles tendon and lower calf muscles and the occurrence of nodes in these areas. The circulation in the dorsalis pedis and posterior tibial vessels should always be tested and the color of the skin noted with the feet elevated and hanging. One should examine the patient for plantar warts and perforating ulcers, which are seen in spina bifida, syphilis, diabetes and syringomyelia.

The height of the arches should be observed and tested for loss of active motion and loss of passive motion; that is, rigidity of any of the joints—toes, forefoot, ankle and subastragalar joints. Limitation of active and passive motion is seen in arthritis, rigid valgus, tuberculosis and infections of the foot. In cases of rigid valgus there is spasm of the peroneal muscles which can be seen and felt. Loss of passive dorsal flexion of the foot with the knee straight is a common finding in normal feet which have an arch higher than the average and is a precipitating factor in foot strain when associated with other conditions that are recognized causes of painful feet. In obscure cases of painful feet a general physical examination should be made and x-ray films of the feet should be taken. Tests of the strength of the muscles controlling the action of the foot are helpful but are not essential.

The old shoes that a patient wears should always be examined, since considerable information can be obtained by noting what happens to the soles, the heels, the counters and the uppers. Persons with short heel cords scuff off the sole at the tip. Pronated feet wear the heels on the inner side. Weak feet that abduct do this, and they also wear the sole away under the great toe joint. When the heads of the middle metatarsals are low a hole is worn in the bottom of the sole. In instances of cock up toes associated with contracted feet the front end of the shoes is apt to turn upward.

The examiner should observe how the patient stands in his shoes. Does he pronate? Is the waist of the shoe on the inner side stretched out and is there a gap between the outer side of the upper and the side of the foot? Do the little toes squat the leather laterally over the outer edge of the sole?

TREATMENT

It must be perfectly obvious, even to the uninitiated, that no special type of shoe can be designed to solve all the difficulties that have been mentioned in this article. The patient should be told to go shopping for a shoe that is comfortable on his feet; then, in most instances, some alteration can be made in that shoe to make it fit more perfectly. This can be brought about in several ways. The heel can be raised all over in order to compensate for the patient's loss of passive dorsal flexion. If there are bunions present, the area over the bunion can be stretched as much as one-half inch if necessary. The shank of the shoe can be brought up to the patient's arch by removing the old shank and inserting a longer, higher shank of untempered steel, which can be raised or lowered, as necessary, until the sole of the shoe is touching the arch of the foot. After a few days' trial, if the shoe is comfortable, the shank is removed and a plaster mold is made of it. The shank is now tempered, refitted to its cast and then placed permanently in the shoe. The cast is kept for future shanks.

When the symptoms of foot strain are more severe it will be necessary to use an arch support made of leather, felt, sponge rubber or metal. There are some fundamental principles involved in fitting supports to painful feet. Elderly persons cannot stand hard supports, and children do better with supports that are flexible. The chief object in fitting a support to a patient's foot is to supply a device which will make a comfortable shoe fit that individual foot more perfectly. The arch support which can be purchased in a store will not answer the purpose for long, because experience has shown that such supports usually furnish only temporary relief from pain. When the pain returns it needs an expert to make further adjustments in any support so that it will continue to give relief as the foot improves. This improvement does not mean that the arch of the foot gets increasingly higher. It does mean that the abnormal position of the foot improves and, as a result, the support no longer fits but must be adjusted; otherwise the patient will be uncomfortable.

Sometimes there is so much pain from foot strain that no form of shoeing or altering of the shoe will give relief. In such instances it is best to keep the patient off his feet entirely until the pain has gone. In most severe cases metal supports are necessary. There are many types and shapes of these, most of which are made from steel hammered by a blacksmith over a plaster cast of the patient's feet. These casts are usually cut so that the arch will conform to the foot. The plate is tempered and applied. It may or may not help. It may have to be hammered up or down so that it will fit better. Hammering tempered steel has the disadvantage that when one hammers it in one place the contours of the whole plate change more or less, so that it is thrown up or down in some places which should not be changed.

There is another disadvantage to cast-made plates and that is that the patient has to wait several days before the plate is ready for trial. I have tried all methods. In the mild cases, removable felt or sponge rubber pads that can be made higher or lower are used. In the more severe cases, steel plates are used and fitted after the method of the late Dr. Robert W. Lovett. These steel arch supports are made on dies in two widths and in varying sizes from 2½ up to 6½. The size of the plate is determined by the position of the front end, which should come just at the neck of the first metatarsal. The support is now adjusted to fit the patient's foot by bending it with a monkey wrench and hammering it on a piece of pig lead so that it will not crack. The bending and hammering go on until the patient says he is comfortable when he stands and walks. He is instructed to wear the supports for two or three hours at a time during the day for a period of a few days and then return for further adjustments, which are always necessary if any improvement takes place.

When complete relief has been obtained, a cast is made of the plate. The plate is tempered, fitted to the cast, covered with leather and given to the patient. It may be necessary to make further slight adjustments, and these are done by hammering the plate on a flat piece of pig lead. When there are symptoms of Morton's toe the untempered plate can be raised locally behind the head of the affected metatarsal until the metatarsalgia disappears. The advantage of this simple method of treating acute foot strain is that the patient leaves the doctor's office treated; in other words there is no waiting. Devices built into the inside of the shoe are used constantly by many surgeons, and with more or less success. However, these devices are difficult to remove from the shoe and are also difficult to alter.

One of the stated objections to the metal plate is that it causes atrophy of the foot. There is no reason to uphold this theory if the foot is properly supported by the shoe and the plate. If the plate is truly a source of atrophy then any supporting device will cause atrophy. Is it not also true that atrophy occurs in the untreated painful foot? In the milder cases of foot strain the shoe recommended for the normal foot will serve, especially if the shank is raised from time to time as improvement of the foot progresses. Raising the inner border of the heel will help to correct the pronated foot and may be incorporated in the methods described.

EXERCISE

To prescribe exercises for a painful, uncomfortable foot which is already overburdened does not seem sound therapy. When the symptoms have been relieved, however, exercises are indicated. They are also indicated in the weak, pronated feet of children and adults. Too many patients become easily discouraged with foot exercises and give them up long before benefit can be expected. The reasons for this are boredom, lack of interest in prolonged treatment and too many exercises to be done at a time. If the exercises can be boiled down to one maneuver, the surgeon will get more cooperation. This one maneuver will increase the tone of all the muscles that control the arch of the foot. The patient is shown how to flex all his toes strongly and at the same time he dorsiflexes, adducts and inverts the foot. This position is held momentarily. The contracted muscles are relaxed slowly and the contractures are repeated several times, morning and evening. One will find that, in the long run, more patients will perform this combined exercise than would do a dozen different exercises ten times each.

Feet which show circulatory disturbances must be shod in such a way that there is no rubbing or undue pressure on any one spot in order to avoid the formation of corns, calluses, abrasions, blisters and gangrene. The underlying condition must be treated when possible. The wearing of proper footgear may postpone amputation of a diabetic leg.

In this article no attempt has been made to discuss the surgical procedures that are applicable to the many complicated foot troubles; i. e. hallux valgus, bursitis, accessory scaphoids and spurs. To do so would involve more than is intended in the mechanical treatment of the painful foot.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

ESTRIOL-ABBOTT (See New and Nonofficial Remedies, 1939, p. 348).

The following dosage form has been accepted:

Capsules Estriol 0.24 mg.: Each capsule contains estriol 0.24 mg. diluted with milk sugar.

SODIUM CACODYLATE (See New and Nonofficial Remedies, 1939, p. 104).

The following have been accepted:

Ampoules Sodium Cacodylate-Upjohn, 0.05 Gm. (¾ grain), 1 cc.
Prepared by the Upjohn Co., Kalamazoo, Mich.
Ampoules Sodium Cacodylate-Upjohn, 0.1 Gm. (1½ grains), 1 cc.
Prepared by the Upjohn Co., Kalamazoo, Mich.
Ampoules Sodium Cacodylate-Upjohn, 0.2 Gm. (3 grains), 1 cc.
Prepared by the Upjohn Co., Kalamazoo, Mich.
Ampoules Sodium Cacodylate-Upjohn, 0.32 Gm. (5 grains), 1 cc.
Prepared by the Upjohn Co., Kalamazoo, Mich.
Ampoules Sodium Cacodylate-Upjohn, 0.45 Gm. (7 grains), 1 cc.
Prepared by the Upjohn Co., Kalamazoo, Mich.
Ampoules Sodium Cacodylate-Upjohn, 0.97 Gm. (15 grains), 2 cc.
Prepared by the Upjohn Co., Kalamazoo, Mich.

The following have been accepted:

Ampuls Sodium Cacodylate-Merrell, 0.05 Gm. (¾ grain), 1 cc.
Prepared by The William S. Merrell Company, Cincinnati.
Ampuls Sodium Cacodylate-Merrell, 0.1 Gm. (1½ grains), 1 cc.
Prepared by The William S. Merrell Company, Cincinnati.
Ampuls Sodium Cacodylate-Merrell, 0.2 Gm. (3 grains), 1 cc.
Prepared by The William S. Merrell Company, Cincinnati.
Ampuls Sodium Cacodylate-Merrell, 0.324 Gm. (5 grains), 1 cc.
Prepared by The William S. Merrell Company, Cincinnati.
Ampuls Sodium Cacodylate-Merrell, 0.454 Gm. (7 grains), 1 cc.
Prepared by The William S. Merrell Company, Cincinnati.

LUNOSOL (See New and Nonofficial Remedies, 1939, p. 457).

The following dosage forms have been accepted:

Unguentum Lunosol 5 Per Cent-Hille.—Lunosol, 5 Gm., incorporated in 95 Gm. of an unguent base composed of 11 Gm. of water, 52.5 Gm. of anhydrous lanolin and 36.5 Gm. of liquid petrolatum in each hundred grams.

Unguentum Lunosol 10 Per Cent-Hille.—Lunosol, 10 Gm., incorporated in 90 Gm. of an unguent base composed of 17.5 Gm. of water, 55.5 Gm. of anhydrous lanolin and 27 Gm. of liquid petrolatum in each hundred grams.

PONTOCAINE HYDROCHLORIDE (See New and Nonofficial Remedies, 1939, p. 73).

The following dosage forms have been accepted:

Ampules Pontocaine Hydrochloride "Niphanoid" for Spinal Anesthesia, 10 mg.: Ampules containing pontocaine hydrochloride in finely divided and instantly soluble form. The trade term "Niphanoid" (from the Greek, "snow like") is applied to the process whereby dilute solutions of the drug are subjected to rapid freezing and subsequent evaporation of the solvent under high vacuum; the resultant material is claimed to be more readily soluble.

Ampules Pontocaine Hydrochloride "Niphanoid" for Spinal Anesthesia, 20 mg.: Ampules containing pontocaine hydrochloride in finely divided and instantly soluble form. The trade term "Niphanoid" (from the Greek, "snow like") is applied to the process whereby dilute solutions of the drug are subjected to rapid freezing and subsequent evaporation of the solvent under high vacuum; the resultant material is claimed to be more readily soluble.

Council on Foods

ACCEPTED FOODS

THE FOLLOWING ADDITIONAL FOODS HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO ACCEPTED FOODS.

FRANKLIN C. BING, Secretary.

FRUIT JUICES INCLUDING TOMATO JUICE (*See* Accepted Foods, 1939, p. 48).

American Grape Juice Corporation, Fredonia, N. Y.

FREEDOM BRAND GRAPE JUICE, sweetened, bottled, pasteurized grape juice prepared from Concord grapes.

Analysis (submitted by manufacturer).—Moisture 82.5%, total solids 17.5%, ash 0.2%, fat negligible, protein (N × 6.25) 0.3%, invert sugar 15.1%, carbohydrates (by difference) 15.8%, titratable acidity as tartaric acid 1.2%; lead (Pb) 0.2 part per million, arsenic trioxide (As_2O_3) less than 0.1 part per million.

Calories.—0.64 per gram; 18 per ounce.

TAFTS BRAND GRAPE JUICE, same as Freedom Brand Grape Juice.

Quaker Maid Company, Inc., New York.

ANN PAGE BRAND TOMATO JUICE.

Analysis (submitted by manufacturer).—Moisture 94.1%, total solids 5.9%, ash 0.9%, sodium chloride (NaCl) 0.6%, fat (ether extract) trace, protein (N × 6.25) 1.0%, reducing sugars as invert 2.6%, carbohydrates other than crude fiber (by difference) 4.0%, acid (as citric) 0.47%, *p*H 4.13, specific gravity at 20 C. 1.025.

Calories.—0.20 per gram; 6 per ounce.

Vitamins.—Chemical titration by the dye method (1938) shows that the product contains 0.2 mg. of ascorbic acid per cubic centimeter, 0.195 mg. per gram, 5.54 mg. per ounce, or 111 international units of vitamin C per ounce.

Rio Grande Valley Citrus Exchange, Weslaco, Texas.

TEXSUN BRAND GRAPEFRUIT JUICE UNSWEETENED.

Analysis (submitted by manufacturer).—Moisture 89.5%, total solids 10.5%, ash 0.3%, fat (ether extract) 0.1%, protein (N × 6.25) 0.4%, sucrose 3.1%, invert sugar 5.1%, crude fiber 0.1%, carbohydrates other than crude fiber (by difference) 9.6%.

Calories.—0.4 per gram; 11.4 per ounce.

Vitamins.—Chemical titration (1938) showed an average of 0.32 mg. vitamin C per cubic centimeter of juice, or 600 international units per hundred cubic centimeters of juice.

GRAIN PRODUCTS (*See* Accepted Foods, p. 97).

The Teichgraeber Milling Company, Gypsum, Kan.

GLORY BRAND CRACKED WHEAT, coarsely ground wheat from which about 3 per cent of the endosperm has been removed.

Analysis (submitted by manufacturer).—Moisture 10.4%, total solids 89.6%, ash 1.6%, fat (ether extract) 1.0%, protein (N × 5.7) 12.1%, crude fiber 3.0%, carbohydrates other than crude fiber (by difference) 71.9%.

Calories.—3.45 per gram; 98 per ounce.

PREPARATIONS USED IN THE FEEDING OF INFANTS (*See* Accepted Foods, 1939, p. 156).

Libby, McNeill & Libby, Chicago.

LIBBY'S BRAND HOMOGENIZED CARROTS.

Analysis (submitted by manufacturer).—Moisture 91.9%, total solids 8.1%, ash 1.2%, sodium chloride 0.6%, fat (ether extract) 0.1%, protein (N × 6.25) 0.8%, crude fiber 0.8%, carbohydrate other than crude fiber (by difference) 5.2%, calcium (Ca) 13.0 mg. per 100 Gm., phosphorus (P) 19.8 mg. per 100 Gm., iron (Fe) 1.0 mg. per 100 Gm., copper (Cu) 0.231 mg. per 100 Gm.

Calories.—0.23 per gram; 6.5 per ounce.

Vitamins.—Protocols of biologic assay (1939) show that the product contains 32.7 U. S. P. units of vitamin A per gram, 927 per ounce; vitamin B_1 is practically absent; less than 0.20 Sherman-Bourquin unit of vitamin G (riboflavin) per gram, less than 5.7 per ounce; and, according to report of chemical titration (1939) 0.39 international unit of vitamin C per gram, 11.2 per ounce.

Merck & Co., Inc., Rahway, N. J.

MERCK MILK SUGAR (LACTOSE U. S. P.).

Analysis (submitted by manufacturer).—Specific rotation at equilibrium +52.2° to +52.5° corresponding to 99.5% lactose. A solution of 1 Gm. of lactose in 20 cc. water is neutral to litmus. Ash not more than 0.1%. Meets U. S. P. tests for heavy metals, dextrose and sucrose. Dextrin and starch absent.

Calories.—About 3.8 per gram; 109 per ounce, depending on the amount of water present.

Mead Johnson & Company, Evansville, Ind.

MEAD'S PECTIN-AGAR IN DEXTRI-MALTOSE, a powdered mixture of Mead's Dextri-Maltose No. 1 (containing 2 per cent sodium chloride).*

Analysis (submitted by manufacturer).—Moisture 2.0%, total solids 98.0%, ash 2.5%, protein (N × 6.25) 1.0%, crude fiber 0.3%, carbohydrates other than crude fiber (by difference) 94.2%.

Calories.—3.5 per gram; 99.3 per ounce.

* Mead's Dextri-Maltose No. 1 with 2 per Cent of Sodium Chloride is described on page 176, Accepted Foods, 1939.
pectin and Agar (U. S. P.).

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, APRIL 20, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.

2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.

3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.

6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.

7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

8. Expansion of public health and medical services consistent with the American system of democracy.

VIRUSES AND THEIR PROPERTIES

The approximate dimensions of many of the viruses now have been determined by careful utilization of methods such as filtration, centrifugation, diffusion and direct microscopic mensuration. Some viruses are relatively large, with diameters of 175 millimicrons; others are of the same order of magnitude as certain protein molecules. The virus of foot and mouth disease, for example, is from 8 to 12 millimicrons in diameter as contrasted with the serum albumin molecule, which has a diameter of approximately 5 millimicrons.[1] Furthermore, information has become available in recent years on the shape, density, electrical charge and cultivation of viruses.

Possibly the most significant development has been in the extension of knowledge of the physical and chemical properties of viruses. The studies of Stanley[2] and his co-workers on the homogeneity of the high molecular weight material isolated from tobacco mosaic diseased plants have been particularly significant. In brief, the experimental results of this work indicate that for practical purposes the crystalline proteins isolated possess the properties of tobacco mosaic virus. Comparison with other purified virus preparations reveals quite different and highly characteristic chemical, physical and serologic properties. Tobacco mosaic virus consists of long rods; treatment with salt or other agents causes two or more of these rods to combine end to end. This phenomenon permits, Stanley believes, a rational explanation of the puzzling filtration behavior of tobacco mosaic virus, which has been reported to have a filtration end point varying all the way from about 13 millimicrons to over 300 millimicrons.

All viruses appear to be or at least to contain nucleoprotein. The ability of organisms to reproduce is associated with nuclear material. Usually it is assumed that the basic unit of this material is a gene, perhaps a single nucleoprotein molecule. Moreover the properties of viruses composed of nucleoprotein are, according to Stanley, essentially the properties which would be postulated for a gene or for a group of genes were they capable of independent existence. The implications of this structural relationship are of great importance in genetics, and the studies which can now be made on virus reproduction and mutation may have a direct bearing on similar events within cells. As pointed out by Mueller,[3] however, there is a great diversity of properties, chemical and physical, manifested by various types of viruses. The inclusion, therefore, of agents differing so widely among themselves is perhaps unfortunate, although any reclassification today could be accomplished only on the basis of size, which would be of little practical value.

The characteristic structure which permits a virus to participate in the metabolic chain of events within cells may be related to the initiation of the cancer process. According to Andrewes,[4] theories about cancer which claim that a virus or viruses enter into the etiology of cancer must postulate that such a virus or viruses are widely distributed in the animal kingdom and that they are normally latent infections but are activated by some stimulus such as the application of a carcinogenic hydrocarbon. Andrewes does not believe that these possibilities can be dismissed lightly, although admittedly there is little concrete evidence that cancer in general is caused in the manner suggested. However, in fowl paralysis, which is certainly related to neoplasms, the causative agent, although not yet demon-

1. Rivers, Thomas M.: Viruses and Virus Diseases, Lane Medical Lectures, Stanford, Calif., Stanford University Press, 1939.

2. Stanley, W. M.: Properties of Viruses, Medicine 18:431 (Dec.) 1939.

3. Mueller, J. Howard: Physical and Chemical Properties of Filtrable Viruses: Virus and Rickettsial Diseases, in Harvard School of Public Health Symposium Volume, Harvard University Press, 1940.

4. Andrewes, C. H.: Latent Virus Infections and Their Possible Relevance to the Cancer Problem, Proc. Roy. Soc. Med. 33:175 (Dec.) 1939.

strated to be a virus, can be transmitted from the mother through the egg. Likewise the development of potent antibodies to the Rous virus by fowls grafted with tar sarcoma offers at least suggestive evidence of some relationship. Finally, the observations of Bittner on breast sarcoma in mice cited by Andrewes and other observations on the so-called toothless viruses suggest some curious if at present still obscure relation to cancerous growth. Little can be added to the summarization by Rivers:

> It is an acknowledged fact that some tumors are caused by viruses; at least, most investigators will admit that some viruses produce hyperplastic growths with all the immediate traits of tumors. Indeed, hyperplasia and necrosis are such important phenomena in the pathological pictures induced by viruses that pertinent remarks had to be made concerning tumors if for no other reason than to emphasize the fact that such disease processes as tumors, warts, measles, fever blisters, smallpox, varicella, poliomyelitis, rabies, yellow fever, fowlpox, foot and mouth disease of cattle, tobacco mosaic, and bacteriophagy, in spite of their striking clinical differences, possess in common characteristic pathological pictures.

Quietly and unostentatiously, painstaking research has gone on in this field. No doubt further information on the nature and properties of viruses will be adapted rapidly to serve the practical needs of preventive and therapeutic medicine.

NEW REGULATIONS ON MEDICINAL FOODS

Beginning on April 29, hearings will be held by the Food and Drug Administration in Washington in order to develop regulations concerning informative labeling of so-called "special purpose" foods with relationship to their vitamin, mineral and other dietary properties. All interested persons are invited to attend these hearings or to send representatives who may wish to present evidence with a view to aiding the Food and Drug Administration in developing suitable regulations. The hearings are being held in accordance with the procedure that has been developed to permit the food industry, consumers and others to offer their views on regulations proposed under the authority granted to the Secretary of Agriculture by the Food, Drug and Cosmetic Act. The regulations to be discussed concern section 403(j) of the act, which deals with foods for special dietary purposes. The mere fact that certain foods may be especially prepared for infants, children, aged persons or persons suffering or convalescing from disease makes them special purpose foods under the law. Preparations especially designed for increasing or decreasing weight or otherwise affecting the structure or functions of the body are also in this category. If a food product is represented for use in the prevention or treatment of disease, it may be subject to the requirements of the regulations.

It is proposed in the new regulations to exempt foods if the vitamins, minerals or other constituents are naturally present in them and not artificially added, or if the foods do not represent extracts, concentrates or other artificial preparations of vitamin, mineral or other dietary factors. Furthermore, it is proposed to exempt foods for which special claims are not made in relationship to such factors. When a food is specifically designed for use in the treatment of various conditions of the type mentioned, it is proposed that its label indicate the dietary properties on which its value for such use is based and that it shall bear on the label directions for use, showing the quantity of the food to be consumed during any one period of one day, also any directions which might involve changes in the quantity of the food to be used when the amounts vary for persons of different ages. However, such labeling and the specific labeling regarding use of such foods for vitamin and mineral content will not apply if the food is to be used only by infants or invalids if the label bears statements showing definitely the quantities of the vitamins present or of minerals or if the label bears a statement that the product is to be used only under the prescription or under the direction of a physician. Furthermore, shipments in bulk of vitamin materials for repackaging are to be exempt.

Special statements are required regarding vitamins with a view to declaring the vitamin content by the common or usual name of each vitamin and indicating clearly what percentage of the minimum daily requirement of each vitamin is supplied by the food in the package. It is proposed that products containing vitamin D bear the statement that there is no special need for this vitamin in the diet provided the skin is adequately exposed to direct sunshine. Furthermore, it is proposed that food products containing vitamins not clearly established as useful or for which a minimum daily requirement has not been established shall bear on the label a statement indicating these facts. The proposed regulations define minimum daily requirements for each vitamin for persons of various ages. Similar statements are proposed regarding minerals in foods, particularly calcium, phosphorus, iron and iodine, with informative statements concerning the minimum quantities of these substances considered necessary as a daily requirement. Infant foods which are represented as substitutes for human milk are to be labeled with percentage statements of moisture, protein, fat and digestible carbohydrates and, if the amounts of certain ingredients are less than are considered desirable, the label is to bear a statement advising the purchaser that additional amounts of this substance must be secured from other sources. Furthermore, there are to be special regulations concerning foods which are believed to have diminished allergenic properties.

The problems raised by these considerations are obviously ones which will have most serious consideration by the medical profession, the officials of the Food and Drug Administration and the manufacturers of both foods and drugs. The difficulty of enlightening the average user as to the extent to which he may employ such materials for purposes of promoting health or the extent to which he must employ them for the cure of a deficiency should be apparent. The problems which confront the Administration are similar to those which have from time to time given serious concern to the Councils on Pharmacy and Chemistry and on Foods of the American Medical Association. The problem may not be a difficult one as far as it concerns foods used in infant feeding or for the diabetic or specifically in relationship to the reduction of weight. When, however, ordinary cereal products may be fortified with what are essentially medicinal doses of iron, calcium or vitamin D, questions are raised which may seriously affect not only the industries concerned in the production of such materials but the health of all the people.

No doubt all these considerations will be presented at the hearings which are to be held in Washington before the suggested findings of fact are issued and the regulations are finally promulgated as an established procedure. In the meantime, it is well to bear in mind the fact that the treatment of disease or of malnutrition with vitamins or mineral salts requires the same type of certainty as to dosage and certainty that the patient receives the materials given that scientific therapy has always demanded. It would be indeed unfortunate if commercial considerations should lead the pharmaceutical industry into the grocery store as an outlet for modern medicaments.

CONTRAINDICATIONS TO ESTROGEN THERAPY

Malignant growths of the mammary gland and the uterus have been induced in rodents with estrogens by numerous investigators. Some physicians, however, have doubted that the therapeutic administration of estrogens in the human being could result in the development of similar malignant growths. It has been pointed out that, theoretically, tremendous dosages of estrogens might be required to induce human cancer, when calculated according to body weight. Furthermore, the scarcity of reports in medical writings on the occurrence of malignant growths following estrogenic therapy has been considered evidence against this possible danger of estrogenic therapy.

No doubt estrogens have been used intensively for relatively too short a time to warrant the conclusion that mere absence of reports from the literature justified a disregard for the possible consequences of estrogenic therapy. Recently two significant reports have appeared which should indicate the possible dangers of administration of estrogens. In this issue of THE JOURNAL, page 1517, is a report by Auchincloss and Haagensen on cancer of the breast possibly induced by estrogenic substance. The case reported is that of a woman with radiation castration, who had a mammary cancer following prolonged use of estrogens. In this case there was a familial history of carcinoma of the breast.

In a recent article, Gemmell and Jeffcoate [1] report that they have observed the appearance of carcinoma of the cervix in three patients among forty-three who were treated with estrogens for kraurosis vulvae and senile vaginitis. The authors state:

> The occurrence of these three cases cannot prove that carcinoma cervicis may be caused by estrogens. But we hope that our experiences will bring the matter to the minds of gynecologists using such endocrine preparations so that similar cases, if they occur, may be reported. They at least point out some practical lessons:
>
> 1. Every patient of menopausal or postmenopausal age, presenting symptoms of discharge, should be subjected to the most careful investigation to exclude carcinoma of the uterus, even when some lesion such as senile vaginitis appears to be the obvious cause. . . .
>
> 2. Estrogens should be administered with caution if the patient has a lacerated or infected cervix or any other precancerous lesion.
>
> 3. Estrogens should probably not be administered to patients with a strong family history of malignant disease.

The Council on Pharmacy and Chemistry and THE JOURNAL have repeatedly warned against the indiscriminate and prolonged use of estrogens and have emphasized the possible occurrence of mammary carcinoma in patients who are susceptible to the development of such malignant growths. It would be unwise to consider that there is safety in using small doses of estrogens, since it is quite possible that the same harm may be obtained through the use of small doses of estrogen if they are maintained over a long period. While there appears little or no evidence to indicate that normal women may develop such malignant growths, it would be well for the physician to realize that this is by no means an impossibility in patients who have a personal or familial history of genital or mammary cancer. It has now become evident that a lacerated cervix may also be a contraindication to intensive estrogenic therapy.

Reports which have appeared are quite appropriate at the present time, as new potent estrogens, easily administered, are being prepared for therapeutic purposes. According to Lipschutz and Vargas,[2] the new synthetic estrogen diethylstilbestrol is far more active than the natural estrogens estrone and estradiol in the production of uterine and extra-uterine fibroids in

1. Gemmell, A. A., and Jeffcoate, T. N. A.: Estrogens and Carcinoma of the Uterus, J. Obst. & Gynaec. Brit. Empire 46:985 (Dec.) 1939.

2. Lipschutz, Alexander, and Vargas, Luis: Tumorigenic Powers of Stilbestrol, Lancet 1:541 (March 23) 1940.

guinea pigs. There is no evidence, however, that it is more carcinogenic than these substances.

It is hoped that it will not be necessary for the appearance of numerous reports of estrogen-induced cancer to convince physicians that they should be exceedingly cautious in the administration of estrogens, which, used correctly, are apparently valuable therapeutic agents.

REORGANIZATION PLAN NO. IV

On April 11 President Roosevelt sent to the Congress Reorganization Plan No. IV, which consolidates certain federal agencies and activities. Certain sections of these proposals are of great interest to the medical profession, particularly as they represent an attempt to gather many widely distributed medical functions into a single agency, as recommended by the American Medical Association in its platform. Thus the President said:

> Federal Security Agency: The Federal Security Agency has as its major purposes the promotion of social and economic security, educational opportunity, and the health of the citizens. The functions of St. Elizabeths Hospital, Freedmen's Hospital, Howard University, and Columbia Institution for the Deaf plainly come squarely within these purposes. Consequently, I find it necessary and desirable in pursuance of the objectives of the Reorganization Act to transfer to the Federal Security Agency the responsibilities of the Interior Department relating to these institutions. The work of St. Elizabeths Hospital and Freedmen's Hospital is much more akin to the activities of the Public Health Service in the Federal Security Agency than to those of any other Federal establishment. Similarly, Howard University and Columbia Institution for the Deaf can derive more benefit from association with the Office of Education in the Federal Security Agency than with any other Federal organization.
>
> I further propose to transfer to the Federal Security Agency the Food and Drug Administration, with the exception of two activities intimately related to the work of the Department of Agriculture. The work of the Food and Drug Administration is unrelated to the basic functions of the Department of Agriculture. There was, however, no other agency to which these functions more appropriately belonged until the Federal Security Agency was created last year. I now believe that the opportunity for the Food and Drug Administration to develop along increasingly constructive lines lies in this new Agency. There is also need for coordination of certain of its functions with those of the Public Health Service. To accomplish these objectives the plan establishes the Administration as a separate unit within the Federal Security Agency.

In concluding his message the President pointed out that "the reorganization plans thus far submitted do not exhaust the transfers, consolidations, and abolitions that may be necessary and desirable." He pointed out also that the act expires on Jan. 20, 1941, and he strongly recommended the reenactment of the Reorganization Act without exemptions so that the structure and management of our government, like the activities and services it performs, might be kept abreast of social and economic change. Perhaps the President has in mind those functions of the Department of Labor particularly concerned with the welfare of mothers and children which belong far more appropriately with the United States Public Health Service.

Current Comment

MEDICINAL EXPORTS IN RECENT MONTHS

Under the international conditions existing at the present time there are few countries in which research, industry and commerce are proceeding normally. Where production is unhampered, business will be greatly accelerated by the concentration of demand to areas functioning in the normal manner. A case in point is the production and export of medicinals by the United States. Long enjoying a favorable position in this field, this country during December 1939 showed an increase of more than 50 per cent in the export of medicinals and pharmaceuticals over that in December 1938, according to the Chemical Division of the United States Bureau of Foreign and Domestic Commerce. An index of the rapid recent acceleration in this trade is provided by the high value of $9,574,000 for the exports during the last four months of 1939, a 63 per cent increase over a similar period of the preceding year. Almost every country and trading area in the world has supported this peak level of foreign demand for American medicinal products (particularly biologic products and unbranded nonproprietaries) since the outbreak of hostilities in Europe.

HIRESTRA LABORATORIES VS. AMERICAN MEDICAL ASSOCIATION

THE JOURNAL published a critical editorial in the issue of April 9, 1938, on "Endocreme," a cosmetic containing the female sex hormone estradiol. On Aug. 18, 1938, the Hirestra Laboratories, Inc., the company which distributed and sold this face cream, filed two suits in the Federal Court at Chicago against the American Medical Association, the editor of THE JOURNAL, and others. One of the suits was in equity and asked for an injunction and damages on the theory that the defendants had conspired to injure the business of the plaintiff. The other suit was in law and asked damages of three million dollars on the theory that the defendants had libeled the plaintiff and had conspired to injure and destroy the business of the plaintiff (the Hirestra Laboratories). The suit in equity was referred to a federal Master in Chancery to hear evidence and report, together with his findings of fact, propositions of law and recommendations in the premises. In the proceedings before the Master in Chancery the plaintiff took the depositions of various witnesses throughout the United States and many witnesses appeared in person. Before the evidence of the plaintiff was concluded before the Master, and about the time the lawsuit was to come on for trial before the Federal Court and a jury, the plaintiff decided to dismiss voluntarily both of the suits. Accordingly, an order was entered on April 5, 1940, in both the suits dismissing them without costs to either party. There was no consideration paid and no promise given by the American Medical Association or the other defendants to induce the dismissal of these suits.

ORGANIZATION SECTION

HOTEL RESERVATIONS FOR THE NEW YORK SESSION

Reservations for the annual session of the American Medical Association in New York are beginning to be received in large numbers. From advance information gathered at medical meetings and from members throughout the United States, the attendance at the New York session will probably surpass even the largest attendance ever recorded at a previous convention of the American Medical Association. The Housing Committee suggests that even though an American Medical Association convention has never been held in a city where so many hotel rooms are available, reservations should be made immediately in order to get accommodations in the hotel desired and at the rate requested.

The low railroad rates as a result of the World's Fair will prove an added attraction and the special American Medical Association days designated by the New York World's Fair on Friday and Saturday, June 14 and 15, are another inducement for attendance at the 1940 convention.

Get your hotel reservations in immediately. See hotel list on page 36 of this issue (April 20).

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—The subcommittee of the Senate Committee on Education and Labor has ordered S. 3230, the Wagner-George hospital construction bill, reported to the full committee with amendments. The full committee, it is understood, will meet April 18 to act on the bill. S. 3633 has passed the Senate, providing that a candidate for appointment in the Dental Corps of the Army, to be eligible, must be a graduate of a recognized dental college, having been engaged in the practice of his profession for at least two years subsequent to graduation, or must have, after such graduation, satisfactorily completed a dental internship of not less than one year in a hospital or dispensary. S. 3654 has passed the Senate, proposing to amend the National Defense Act so as to provide that the authorized maximum number of enlisted men of the Medical Department of the Regular Army shall be in each fiscal year such number as shall equal 7 per cent of the average annual pay strength of the active list of the Regular Army and the average strength of all other military personnel on extended active duty with the Regular Army during such fiscal year.

Bills Introduced.—President Roosevelt, on April 11, submitted to the Congress Reorganization Plan No. IV. This plan proposes, among other things, to transfer to the Federal Security Agency the Food and Drug Administration, except those functions relating to the administration of the Insecticide Act of 1910 and the Naval Stores Act, which remain in the Department of Agriculture. The plan also proposes to transfer to the same Agency St. Elizabeths Hospital, Freedmen's Hospital, Howard University and Columbia Institution for the Deaf. S. 3728, introduced by Senator Johnson, California, proposes that all persons who served in a civilian capacity under the jurisdiction of the Quartermaster General during the War with Spain, the Philippine Insurrection or the China Relief Expedition on vessels owned by the United States and engaged in the transportation of troops, supplies, ammunition or materials of war and who were discharged for disability incurred in such service shall be entitled to medical and hospital treatment and domiciliary care in Veterans' Administration facilities in the same manner and to the same extent as now or hereafter provided for veterans of any war.

DISTRICT OF COLUMBIA

Bill Introduced.—H. R. 9284, introduced by Representative Rayburn, Texas, provides for the issuance of a license to practice the healing art in the District of Columbia to Dr. A. L. Ridings, formerly of Sherman, Texas.

STATE MEDICAL LEGISLATION

Mississippi

Bill Passed.—H. 914 passed the House April 11, proposing to appropriate $100,000 to the state board of health for the fiscal years 1940 and 1941 to conduct a program of eradication and control of venereal disease.

Bills Introduced.—H. Res. 32 proposes a minimum increase in the appropriation for hospitalization for the indigent sick for the 1940-1941 biennium of $500,000 over the appropriation for the same purposes made for the 1938-1939 biennium. H. 816 proposes to establish a state charity hospital and nurse's home in north Mississippi in or near New Albany, Union County.

WOMAN'S AUXILIARY

California

An auxiliary to the Sonoma County Medical Society was organized November 16 and an auxiliary to the Kings County Medical Society December 11.

The November meeting of the auxiliary to the Alameda County Medical Association was held in Oakland. Mr. Elwood A. Stevenson, superintendent of the School for the Deaf, talked on "Educational Procedure with the Deaf Child."

The auxiliary to the Fresno County Medical Society raised $40 to place subscriptions to *Hygeia* in public reading rooms in Fresno County.

Mrs. Rollo K. Packard, president of the auxiliary to the American Medical Association, was a guest of the auxiliary to the Los Angeles County Medical Association at a Christmas tea at the home of Mrs. E. Eric Larson in Los Angeles December 19.

A joint meeting of the auxiliaries to the Monterey and the San Benito county medical societies was held in Salinas December 7. A program was presented on *Hygeia* and the subjects selected from the magazine were the history of blood transfusions, the history of treatment for cholera, and environment and heredity.

Iowa

The auxiliary to the Dallas-Guthrie County Medical Society met in Adel January 18. A paper on "Mental Hygiene" was read by Mrs. Elwyn Butterfield.

At the January meeting of the auxiliary to the Madison County Medical Society members voted to place *Hygeia* in

the Truro and St. Charles schools. A paper on "Mental Hygiene" was read by Drs. J. F. Veltman.

Mrs. E. A. Hanske, president of the auxiliary to the Iowa State Medical Society, spoke on "The Functions of the Auxiliary" at a meeting of the auxiliary to the Pottawattamie County Medical Society in Council Bluffs January 16.

The auxiliary to the Woodbury County Medical Society entertained the wives of the doctors attending the two day meeting of the Sioux Valley Medical Association in Sioux City, January 17-18.

South Dakota

The South Dakota Medical Auxiliary will celebrate its thirtieth anniversary at Watertown, May 21-22, at the time the state medical association holds its annual meeting.

The South Dakota Medical Auxiliary was organized Sept. 29, 1910. Mrs. R. D. Jennings, Hot Springs, S. D., the first president, still resides in Hot Springs. Membership in 1910 was eighteen; in 1939 membership was 134. All the doctors' wives in the state are cordially invited to the anniversary meeting in Watertown, May 21 and 22. The program for the year is as follows:

1. Organizing new districts.
2. Promoting health education by means of *Hygeia* and the study of state health laws cooperating with the parent-teachers associations and other women's organizations.
3. Studying the lives of distinguished men and women in medical work.
4. Observing Doctors' Day.
5. Donations for the Medical Benevolence Fund.
6. Cooperation with the A. M. A. in promoting the medical radio programs.

At a meeting of the fourth district medical auxiliary at the home of Mrs. Ola Stout, Pierre, March 15, Mrs. B. M. Hart, Onida, was elected president; Mrs. I. R. Salliday, Pierre, vice president, and Mrs. M. M. Morrissey, Pierre, secretary-treasurer.

Tennessee

Dr. L. W. Edwards, chairman of the Committee on Public Policy and Legislation, Tennessee State Medical Association, spoke on the Wagner Bill at the January meeting of the auxiliary to the Nashville Academy of Medicine and Davidson County Medical Society. The auxiliary sponsored a program given at the Woman's Civic Forum recently; Dr. Willis H. Thompson spoke on "The Children's Charter."

At a meeting of the auxiliary to the Stones River Academy of Medicine, Murfreesboro, Mrs. Earl Roberts read a paper on "Some Medical References in Shakespeare."

Wisconsin

At a meeting of the auxiliary to the Columbia-Marquette-Adams County Medical Society the booklet, "The Doctor's Wife," by Dr. Rock Sleyster, was read.

At the December meeting of the auxiliary to the Dane County Medical Society in Madison Mr. Alfred Ingersoll spoke on his experiences with the youth groups in Germany, France, Belgium and Holland.

Mr. Phil Grau spoke on "What's Behind the News?" at an evening meeting of the auxiliary to the Milwaukee County Medical Society in Milwaukee February 12.

Dr. William A. O'Brien, of the University of Minnesota, spoke on "Socialized Medicine" at a meeting of the auxiliary to the Polk County Medical Society in Osceola December 14.

Dr. J. W. McRoberts spoke on the life of Sir William Osler at the January meeting of the auxiliary to the Sheboygan County Medical Society in Sheboygan. Members of the auxiliary have raised funds to place *Hygeia* in the schools of Sheboygan County.

MEDICAL ECONOMIC ABSTRACTS

ERRORS IN INFANT MORTALITY RATES

The rate of infant mortality is usually given as the number of deaths under 1 year per thousand live births. In any ratio such as this, inaccuracy in the number either of births or of deaths reported has an important effect on the ratio. A study by the Bureau of the Census, November 10, on "Birth Test Surveys," covering samples of counties in Georgia and one county in Maryland, shows that in certain classes of the population in Georgia only from 50 to 84 per cent of the total actual births were registered. Even in the classes having what is designated as "superior registration," which includes those in large cities, hospitalized, attended by a physician, the more intelligent and the well-to-do, the percentage of births registered was between 83 and 98, the latter figure applying only to hospitalized births.

The study does not attempt to estimate the extent to which incomplete birth registration prevailed or to give any average figure which might be applied to the entire state. It is evident however that, if the conditions shown in twenty-six Georgia counties does represent a fair sample, the average of registered births would be not far from 80 per cent. In other words, it would appear that the figures given for infant mortality in the state of Georgia were not the "deaths under 1 year per thousand live births" but rather the deaths in about 1,200 live births.

It is unsafe to assume that any such conditions exist uniformly throughout the United States or in states with well organized health departments, long established systems of registration, higher economic conditions and more extensive hospitalization. However, it is true that the highest recorded infant death rates are found in just the states where the conditions that accompany imperfect registration are most common. It is not suggested that the variations in published infant mortality rates are due entirely or even principally to statistical defects. It is, however, certain that the recorded infant mortality rate would be reduced by complete birth registration. It is even possible that such an administrative and statistical change might produce greater improvements in this particular type of vital statistics than some of the schemes that are urged for the provision of medical care.

REHABILITATION IN WEST VIRGINIA

A description of the plan originated by the West Virginia State Medical Association, in cooperation with the Department of Public Assistance, for rehabilitation of the "unemployable" on the public relief rolls was given in a previous issue of THE JOURNAL.[1]

The progress in the current year has extended the scope of the plan.[2] The program was proceeding so well that its provisions were written into a new West Virginia Public Assistance Law. This legislation instituted a program which got under way as a regularly established service Feb. 1, 1937. A committee of the state medical association, in cooperation with the Department of Public Assistance, approved the physicians qualified to perform the necessary surgery and prosthetic work. Up to June 1939 physical rehabilitation under this program was provided for 3,420 persons suffering from twenty-six different kinds of handicaps—these ranged all the way from bad teeth to hernia.

During this period $306,029.42 was expended for the following items:

Surgery fees	$123,365.98
Hospital fees	134,680.15
Prosthetic appliances	47,983.29

The average cost per case was $92.54. Of the 3,420 persons physically rehabilitated 2,664, or 77.9 per cent of the total, were returned to employment. The number able to return to employment but not employed June 30, 1939, was 756, or 22.1 per cent of the total. The records show that 1,882, or 70.6 per cent of the persons rehabilitated, were placed in private employment; 740, or 27.8 per cent with the WPA, fifteen, or 0.6 per cent, with the NYA, and twenty-seven, or 1 per cent, with the CCC.

It is estimated that this rehabilitation program saved $900,000 which would otherwise have had to be spent for general relief.

1. West Virginia's Adult Physical Rehabilitation Program, J. A. M. A. 111:1105 (Sept. 17) 1938.
2. Power, F. Ray: Implications for Vocational Rehabilitation Found in Recent Legislation Concerning Physical Restoration, National Rehabilitation News 3:2 (Feb.) 1940.

Medical News

(Physicians will confer a favor by sending for this department items of news of more or less general interest: such as relate to society activities, new hospitals, education and public health.)

CALIFORNIA

The George Dock Lectureship Created.—The Walter Jarvis Barlow Society of the History of Medicine has created a lectureship in honor of Dr. George Dock, since 1932 honorary professor of medicine, University of Southern California School of Medicine, Los Angeles. Dr. Dock presented the first lecture at a dinner observing his eightieth birthday, April 2. His subject was "A Dictionary of Medical Biography." Dr. Dock graduated at the University of Pennsylvania School of Medicine, Philadelphia, in 1884. He has served on the staffs of his alma mater, University of Texas Medical Department, Galveston, University of Michigan Medical School, Ann Arbor, Tulane University of Louisiana School of Medicine, New Orleans, and Washington University School of Medicine, St. Louis. He was a member of the California State Board of Medical Examiners from 1930 to 1932 and president of the Association of American Physicians, 1916-1917.

FLORIDA

State Medical Meeting in Tampa.—The sixty-seventh annual meeting of the Florida Medical Association will be held at the Tampa Terrace Hotel and the Chamber of Commerce Building, Tampa, April 29-May 1, under the presidency of Dr. Leigh F. Robinson, Fort Lauderdale. The speakers will include:

Dr. Warren W. Quillian, Coral Gables, Infection of Nasal Accessory Sinuses in Childhood.
Dr. Ludo von Meysenbug, Daytona Beach, Management of the Breast Fed Baby, Including Immunization Procedures.
Drs. Hermon Marshall Taylor, Lucien V. Dyrenforth, Jacksonville, and Cash B. Pollard, Ph.D., Gainesville, Absorption of Quinine into the Cerebrospinal Fluid of the Fetus in Utero.
Dr. Henry E. Palmer, Tallahassee, Impetigo Contagiosa Complicated by Hemorrhagic Nephritis.
Dr. Edwin Laurence Scott, Ocala, The Medical Man and the Workmen's Compensation Law.
Dr. Donald Paul Bird, Lakeland, A Consideration of Climate and Altitude in the Treatment of Hypertension and Myocardial Failure.
Dr. John W. Snyder, Miami, Chronic Empyema.
Drs. Lawrence H. Kingsbury and William O. Fowler, Orlando, Thoracoplasty Program at the Florida Tuberculosis Sanatorium; Preliminary Report.
Drs. Louis M. Orr and Palmer R. Kundert, Orlando, Therapeutic Evaluation in Cases of Cryptorchidism.
Dr. Claude G. Mentzer, Miami, Metycaine as a Caudal Anesthetic in Proctologic Surgery; Report of 100 Cases.
Dr. James G. Lyerly, Jacksonville, The Syndrome of the Dislocated Intervertebral Disk.
Dr. Alan D. Brown, Jacksonville, Experimental Atabrine Therapy in Granuloma Inguinale.
Dr. Albert B. McCreary, Jacksonville, Medicine, Public Health and Local Government.
Dr. Nelson M. Black, Miami, Compensation in Industrial Ophthalmology.
Dr. Alfred G. Levin, Miami, Role of X-Ray Therapy in Nonmalignant Disease.

Dr. Byrl R. Kirklin, Rochester, Minn., will address one session on "Bleeding Lesions of the Gastrointestinal Tract." A symposium on heart disease will be presented by Drs. Roscoe H. Knowlton, St. Petersburg; Turner Z. Cason, Jacksonville, and Edward Sterling Nichol, Miami. Other societies meeting at this time include the Florida Railway Surgeons Association, Florida Pediatric Society, Florida Radiological Society, Florida Internists' Society, Florida Society of Dermatology and Syphilology, Florida Society of Ophthalmology and Otolaryngology, Florida Association of Industrial Surgeons and the health officers' section of the Florida Public Health Association.

IOWA

State Medical Meeting in Des Moines.—The eighty-ninth annual session of the Iowa State Medical Society will be at the Hotel Fort Des Moines, Des Moines, May 1-3, under the presidency of Dr. Felix A. Hennessy, Calmar. General sessions will be addressed by:

Dr. Wyman C. C. Cole, Detroit, Etiology and Significance of Asphyxia of the Newborn.
Dr. Arthur E. Hertzler, Halstead, Kan., Principles of Peritoneal Drainage.
Dr. John DeJ. Pemberton, Rochester, Minn., Present Status of Surgery of the Spleen.
Dr. Albert M. Snell, Rochester, Minn., Deficiency States and Their Treatment.
Dr. Marvin F. Jones, New York, Trouble Shooting.
Dr. Alphonse McMahon, St. Louis, subject not announced.

The guest speakers will also participate with Iowa physicians in the sectional conferences which make up the program Wednesday and Thursday afternoons. Dr. Hans Brunner, Chicago, will conduct a clinic before the eye, ear, nose and throat section Thursday morning. A smoker will be held Wednesday evening and the annual banquet Thursday evening. Other societies meeting during this time will include the State Society of Iowa Medical Women, May 1, under the presidency of Dr. Gail A. McClure, Ames, and the Iowa State Pediatric Society, April 30. Included among the speakers at the latter meeting will be Dr. Aladar Farkas, Budapest, Hungary, visiting professor of orthopedics, State University of Iowa College of Medicine, Iowa City, whose subject will be "Pathogenesis of Scoliosis in Children." The woman's auxiliary to the state medical society will hold its eleventh annual meeting at the Hotel Savery, May 1.

LOUISIANA

State Medical Meeting in New Orleans.—The sixty-first annual meeting of the Louisiana State Medical Society will be held at the Roosevelt Hotel, New Orleans, April 22-24, under the presidency of Dr. Dorman B. Barber, Alexandria. Out of state speakers will include:

Dr. Wendell McLean Long, Oklahoma City, Uterine Bleeding.
Dr. Byrl R. Kirklin, Rochester, Minn., Solving Problems in the Diagnosis of Diseases of the Lungs.
Dr. Howard K. Gray, Rochester, Significance and Surgical Treatment of Ulcerating Lesions of the Stomach.

Annual orations will be delivered by Governor-Elect Sam Houston Jones, Lake Charles, and Dr. Rudolph Matas, New Orleans. Louisiana physicians on the general program will include:

Dr. John H. Musser, New Orleans, Typhus Fever in Louisiana.
Dr. Eugene M. Robards Jr., Jackson, Estrogenic Hormone Therapy in the Treatment of Presenile and Manic Depressive Psychosis.
Dr. Edmund M. Connely, New Orleans, Present Status of Therapeutic Shock in Psychiatry.
Drs. Daniel N. Silverman and Roy J. St. Martin, New Orleans, Early Diagnosis and Treatment of Amebic Abscess of the Liver.
Dr. Lucian W. Alexander, New Orleans, A Preliminary Report of the Use of Prostigmine Methylsulfate in Deafness.
Drs. Edward William Alton Ochsner and Michael E. DeBakey, New Orleans, Carcinoma of the Lung.

The Louisiana State Pediatric Society will hold its twelfth annual meeting at the Roosevelt Hotel, April 22, under the presidency of Dr. Philip C. DeVerges, New Orleans. Dr. Julius Bauer, clinical professor of medicine, Louisiana State University School of Medicine, New Orleans, will speak on "Obesity in Childhood." At the evening session Dr. Bauer will discuss "Pseudo-Endocrine versus Endocrine Conditions in Childhood." Other societies meeting during the annual session of the state medical society include the Louisiana Gynecological and Obstetrical Society, the Louisiana Coroners' Association, the Louisiana branch of the National Gastro-Enterology Society and the Louisiana-Mississippi Ophthalmological and Otolaryngological Society. There will also be a meeting of the regional fracture committee of the American College of Surgeons.

MASSACHUSETTS

Psychiatric Meeting.—The annual session of the New England Society of Psychiatry will be held at the Danvers State Hospital, Hathorne, April 25, under the presidency of Dr. Charles H. Dolloff, Concord, N. H. The speaker will be Dr. Moses Ralph Kaufman, Boston, and his subject, "Factors in Psychotherapy: A Psychoanalytic Evaluation."

Course on Industrial Medicine.—The Harvard University School of Public Health, Boston, is sponsoring a course in industrial medicine to be held in May. Clinics, lectures and plant visits will cover various aspects of industrial medicine and surgery. Additional information may be obtained from Dr. Cecil K. Drinker, dean of the Harvard School of Public Health, 55 Shattuck Street, Boston.

MINNESOTA

Annual Lecture on Cancer.—John J. Bittner, Ph.D., of the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine, will deliver the annual George Chase Christian Lecture of the Cancer Institute of the University of Minnesota, Minneapolis, April 30. His subject will be "Breast Cancer as Influenced by Nursing."

Society News.—Dr. Joseph Brennemann, Chicago, addressed the Hennepin County Medical Society in Minneapolis, April 1, on acute conditions of the abdomen in the child.——The Minneapolis Surgical Society was addressed, April 4, among others, by Drs. Arthur F. Bratrud on "Meckel's Diverticulum Containing Pancreatic Tissue" and Frederick A. Olson, "Avulsion of the Insertion of the Biceps Brachii Tendon."——Dr. Moses Barron, Minneapolis, discussed "Some Uses of Sulfamidopyridine Preparations in the Treatment of Infectious Diseases" before the Minnesota Academy of Medicine in St. Paul, April 10, and Dr. Robert G. Green, Minneapolis, "Modifications of Viruses for Vaccines."——René J. Dubos, Ph.D., Rockefeller Institute for Medical Research, New York, gave a Mayo Foundation lecture, April 8, on "Studies on the Protective Substances Elaborated by the Soil Bacillus."

MISSOURI

State Medical Meeting in Joplin.—The eighty-third annual session of the Missouri State Medical Association will be held at the Hotel Connor, Joplin, April 29-May 1, under the presidency of Dr. James R. McVay, Kansas City. The Jasper County Medical Society will be host. Out of state speakers will include:

Dr. Heyworth N. Sanford, Chicago, Studies in Blood Coagulation Disturbances.
Dr. John W. Harris, Madison, Wis., Pain Relief in Labor.
Dr. Louis A. Buie, Rochester, Minn., Office and Hospital Management of Some Anorectal Disorders.
Dr. Cyrus C. Sturgis, Ann Arbor, Mich., Prognosis and Treatment of Hypertension.
Dr. Alfred I. Folsom, Dallas, Texas, The Role of the Female Urethra in Bladder Irritation in Women.
Dr. Joseph W. Gale, Madison, Wis., Acute Suppurative Pleurisy.
Dr. Everett D. Plass, Iowa City, Functional Menstrual Disturbances.
Dr. George W. Post, Chicago, Importance of Water Balance and the Electrolytes in the Preoperative and Postoperative Care of Surgical Patients.
Dr. John H. Musser, New Orleans, Treatment of Some of the Contagious Diseases.

A dinner in honor of past presidents of the association will be held Monday evening. Dr. Nathan B. Van Etten, New York, President-Elect, American Medical Association, will be the speaker; his subject will be "An American Health Program." A round table discussion on "Problems in the Practice of Medicine" will be a feature of the dinner meeting. A round table luncheon will be held Tuesday with Dr. Gale discussing surgery; Dr. Sturgis, internal medicine, and Dr. Folsom, urology. One on Wednesday will be addressed by Dr. Post on surgery; Dr. Musser, internal medicine; Dr. Plass, obstetrics and gynecology, and Dr. John Aull, Kansas City, pediatrics. On the first day of the annual meeting the maternal welfare committee will hold a special session with Dr. Harris presenting a "Critique of Report of Maternal Death and Discussion of Submitted Questions."

NEVADA

Annual Registration Due May 1.—All persons holding licenses to practice medicine in Nevada are required by law to pay annually to the treasurer of the board of medical examiners, on or before May 1, a tax of $2. Failure to do so operates to forfeit a licentiate's right to practice medicine, and his license to practice can be reinstated thereafter only on the payment of a $10 penalty.

NEW YORK

Anatomist Goes to Carnegie Laboratory.—Robert K. Burns Jr., Ph.D., associate professor of anatomy at the University of Rochester School of Medicine and Dentistry, Rochester, has been appointed research professor on the staff of the embryology laboratory of the Carnegie Institution of Washington. The laboratory is in Baltimore. Dr. Burns took his doctorate at Yale University in 1924 and taught at the University of Cincinnati before joining the Rochester faculty. Dr. George W. Corner, professor of anatomy and curator of the medical library at Rochester, was recently appointed director of the Carnegie laboratory. He and Dr. Burns will assume the new positions in July.

New York City

Chemist Honored for Research on Enzymes.—John M. Nelson, Ph.D., professor of chemistry at Columbia University since 1920, received the William H. Nichols Medal of the New York section of the American Chemical Society at a meeting March 8. Dr. Nelson was cited as an "internationally recognized authority on the isolation and purification of naturally occurring enzymes and the quantitative study of their modes of action."

Ledyard Fellowships Awarded.—Two fellowships, one for 1939 and one for 1940, have been awarded by the New York Hospital from a fund established by Mrs. Ruth E. Ledyard in memory of her husband, the late Lewis Cass Ledyard Jr., a governor of the hospital. The awards went to Dr. Willis Fiske Evans, Richmond, Va., for research on the peripheral blood flow and Dr. Charles O. Warren Jr., Boston, to continue research on the physiology of the bone marrow. Both are currently working at Cornell University Medical College.

Alumni Day at Long Island College.—Alumni Day will be observed at Long Island College of Medicine on April 27. Round table discussion will be held on anatomy, chemistry, obstetrics and gynecology, pathology, pediatrics, physiology, surgery, radiology and gastro-enterology. The program also includes a symposium on pneumonia. At the luncheon Dr. Henry M. Moses, colonel, medical reserve corps, U. S. Army, among others, will discuss "The Medical Profession in a National Emergency." The annual banquet will be addressed by Dr. Frank L. Babbott, president, Long Island College of Medicine, and Dr. Dallas G. Sutton, captain, medical corps, U. S. Navy.

Dr. Emerson to Retire from DeLamar Institute.—Dr. Harry Stoll Mustard, Hermann M. Biggs professor of preventive medicine, New York University College of Medicine, has been appointed director of the DeLamar Institute of Public Health at Columbia University to succeed Dr. Haven Emerson, who plans to retire July 1. Dr. Mustard will also be professor of public health practice. Dr. Mustard has served on the faculty of the Medical College of South Carolina, where he graduated in 1911; as health officer of Preston County, W. Va.; assistant commissioner of health of Tennessee; associate professor of public health administration, Johns Hopkins University School of Hygiene and Public Health, Baltimore, and lecturer in the school of medicine. Dr. Mustard also served as chief medical officer of the Muscle Shoals Sanitary District and executive officer of the department of sanitation, Emergency Fleet Corporation. He has been at New York University since 1937. He is 51 years of age and a native of Charleston, S. C. He is a member of the board of scientific directors of the International Health Division of the Rockefeller Foundation and of the public health committee of the Commonwealth Fund. Born in New York, Dr. Emerson graduated at Columbia University College of Physicians and Surgeons in 1899. He was a member of the teaching faculty of his alma mater from 1902 to 1914; president of the board of health and commissioner of the city department of health from 1915 to 1917 and professor of preventive medicine at Cornell University Medical College 1920-1921. He has been professor of public health administration at Columbia since 1922. Dr. Emerson is well known for his direction of health and hospital surveys. He is a member of the National Advisory Health Council of the U. S. Public Health Service and a past president of the American Public Health Association. He is 65 years of age.

OHIO

Society News.—Dr. Elmer L. Sevringhaus, Madison, Wis., addressed the Columbus Academy of Medicine, March 18, on "Endocrine Therapy in General Practice."——Dr. Ira D. Baxter, Lima, addressed the Logan County Medical Society, Bellefontaine, March 1, on surgical conditions of childhood.——Dr. Samuel Iglauer, Cincinnati, addressed the Hempstead Academy of Medicine, March 11, on "Bronchoscopy and Esophagoscopy."——Dr. Samuel L. Siegler, Brooklyn, addressed a special meeting of the Stark County Medical Society, Canton, recently on "Pregnant Mare Serum for Treatment of Ovarian and Testicular Dysfunction."

Practitioner Honored.—The Tuscarawas County Medical Society gave a dinner, March 6, at Uhrichsville, in honor of Dr. James A. McCollam, who has practiced fifty years in the town. Among speakers who paid tribute to Dr. McCollam were Drs. Glenn I. Goodrich, Dover, president of the county society; Jay W. Calhoon, Uhrichsville; Jonathan Forman, Columbus, editor of the *Ohio State Medical Journal*, and Mr. Charles S. Nelson, executive secretary of the Ohio State Medical Association. The society presented to Dr. McCollam a book containing autographs of most of the physicians in the county. Dr. McCollam has served as president of the county society. He was the first health commissioner of Uhrichsville, according to the Dover *Reporter*, and has been active in religious and civic affairs. He graduated from the old Starling Medical College, Columbus, in 1890.

OKLAHOMA

Pneumonia Control Program.—Laboratory service, serums and sulfapyridine have recently been made available to Tulsa and Oklahoma City through the cooperation of the Tulsa and Oklahoma county medical societies, the state health department and the department of bacteriology of the University of Oklahoma School of Medicine. The facilities have been furnished free to those unable to pay for them and unable to obtain them elsewhere.

PENNSYLVANIA

Society News.—Dr. William W. G. Maclachlan, Pittsburgh, discussed treatment of pneumonia at a meeting of the Fayette County Medical Society, Uniontown, April 4. —— A discussion of "Geriatrics" featured a meeting of the Shenandoah Medical Society, March 11, with the following speakers: Drs. John S. Monahan, Saul Supowitz, Stanley W. Stanulonis and Elinor M. Langton, Shenandoah; Peter J. Kapo and Roland F. Fleck, Mahanoy City.——Dr. William Bates, Philadelphia, addressed the Northampton County Medical Society, Easton, March 15, on "Parietal Versus Visceral Pain and Tenderness."

Pittsburgh

Annual Surgical Meeting.—Drs. Kellogg Speed, Chicago, and Robert M. Zollinger, Boston, will be guest speakers at the annual meeting of the Pittsburgh Surgical Society, April 25, on "Injuries of the Carpal Bones" and "Surgical Treatment of Gastric and Duodenal Ulcers" respectively. The meeting will be preceded by a banquet in honor of the guest speakers.

RHODE ISLAND

Personal.—Dr. William Hindle, Providence, has been appointed superintendent of the Charles V. Chapin Hospital, Providence, to succeed Dr. Dennett L. Richardson, who recently became superintendent of the Rhode Island Hospital.

Society News.—Dr. Burton E. Hamilton, Boston, addressed the Providence Medical Association, April 1, on "Heart Disease in Pregnancy." Dr. Frederick C. Irving, Boston, discussed the paper. Dr. Samuel F. Marshall, Boston, addressed the association, March 4, on "Management of Peptic Ulcer and Its Surgical Aspects."

TENNESSEE

Meetings of Specialists.—The Tennessee Academy of Ophthalmology and Otolaryngology held its annual meeting in Chattanooga, April 9, in conjunction with the annual meeting of the Tennessee State Medical Association. Guest speakers were Drs. Harry S. Gradle, Chicago, on "Secondary Glaucoma" and Albert C. Furstenberg, Ann Arbor, Mich., "Acute Infections of the Mouth, Pharynx, Cervical Region and Mediastinum."——The Tennessee State Pediatric Society held its annual meeting April 9. Guest speakers included Drs. Harry S. Andrews, Louisville, Ky., on "Laryngotracheobronchitis"; Willis H. Thompson, Minneapolis, "Vitamin K and Prothrombin Deficiency in the Newborn," and Mynie G. Peterman, Milwaukee, who addressed a joint meeting with the state medical association on "Convulsions in Children and Their Etiology and Treatment."

TEXAS

Society News.—Dr. James K. Howles, New Orleans, addressed the Jefferson County Medical Society, Port Arthur, recently on "Diagnosis and Treatment of Syphilis."——Drs. Elmer R. Hayes and Orman H. Trimble, Greenville, addressed the Hunt-Rockwall-Rains Counties Medical Society recently on "Differential Diagnosis in Jaundice" and "Leukemia" respectively.

Physicians Honored for Charity Service.—Mr. Ben Taub, chairman of the board of directors of Jefferson Davis Hospital, Houston, recently gave a dinner in honor of seven physicians who have served the clinics of the charity hospital for the past two decades, marking their retirement from an active to an honorary status. The physicians were Drs. Leonardo Allen, Joseph Allen Kyle, John Mark O'Farrell, John T. Moore, Seeley T. Pulliam, Martin J. Taylor and Elva A. Wright. Each received an inscribed key.

Waco Opens City Hospital.—A hospital to care for indigent patients was opened in Waco recently under the auspices of the city and the McLennan County Medical Society. With a charitable bequest, the city bought the former Colgin hospital and clinic building for $45,000 and spent about $12,000 for repairs and equipment, it is reported. The medical society will staff the new hospital, taking turns in the clinics and on the ten medical services. The first floor will be used for clinics; the second will be devoted to the surgical department, isolation ward and a ward for Negroes, and the third floor has accommodations for white patients, with twenty-five beds.

WISCONSIN

The William Snow Miller Lecture.—Dr. Esmond R. Long, director of the Henry Phipps Institute, University of Pennsylvania, Philadelphia, delivered the thirteenth annual William Snow Miller Lecture at the University of Wisconsin, Madison, March 25, under the auspices of Phi Beta Pi. Dr. Long's subject was "The Decline of Tuberculosis with Special Reference to Its Generalized Form."

Personal.—Citizens of Ashland held a testimonial dinner recently for Dr. John M. Dodd Sr., who has practiced in the town for many years. Dr. Dodd was the first secretary of the Ashland County Medical Society, a councilor of the state medical society from 1903 to 1930, a member of the state board of medical examiners from 1913 to 1924 and president of the state society in 1912. He received the council award of the state society in 1930.

Society News.—Dr. Archibald L. Hoyne, Chicago, addressed the Dane County Medical Society, Madison, March 12, on "Significant Signs in Contagious Diseases." —— Drs. Malcolm M. Hargraves and Fred Z. Havens, Rochester, Minn., addressed the Chippewa County Medical Society, Chippewa Falls, March 12, on "The Practical Relationship of Hematology to Internal Medicine" and "Treatment of Cancer of Face, Lips and Oral Cavity" respectively.——Dr. Richard Bardon, Duluth, Minn., addressed the Douglas County Medical Society, Superior, March 6, on "Ulcerated Colitis."——Dr. Edward L. Tharinger, Milwaukee, addressed the Washington-Ozaukee Counties Medical Society, West Bend, recently on "Criminology and the Doctor." —— A program on tuberculosis was presented at a meeting of the Racine County Medical Society, Racine, March 21, by Drs. Cornelius A. Harper, Madison, state health officer; Arthur A. Pleyte, Milwaukee; George N. Gillett and Carl O. Schaefer, Racine.——Dr. Nathan S. Davis III, Chicago, addressed the Rock County Medical Society, Beloit, recently on "Can the Government Render Efficient and Satisfactory Medical Service?"

PUERTO RICO

Health Department Opens Children's Home.—The department of health of Puerto Rico inaugurated its new Rafael Martinez Nadal Insular Home for Children at Guaynabo, March 3. The new school, which accommodates about 400 children, has modern vocational education facilities.

University News.—Magnus I. Gregersen, Ph.D., New York, gave an address at the School of Tropical Medicine, University of Puerto Rico, San Juan, February 29, on "The Relations of Thirst to Salt and Water Balance." Drs. Juan A. Pons and Thomas D. Slagle, San Juan, spoke at the seminar, February 8, on thyroid disease in Puerto Rico.

GENERAL

American Pediatric Society.—The fifty-second annual meeting of the American Pediatric Society will be held at Skytop, Pa., May 2-4, under the presidency of Dr. Herbert B. Wilcox, New York. Among the speakers will be:

Dr. Randolph K. Byers, Boston, Certain Reactions of Children with Head Injuries.

Dr. George M. Guest and S. Rapoport, Cincinnati, Studies of Acid-Soluble Phosphorus Compounds of Red Blood Cells in Diabetic Acidosis.

Dr. Alexis F. Hartmann, St. Louis, and Miss Anne M. Perley, Observations on Sulfamethylthiazole.

Drs. Alfred T. Shohl, Kenneth D. Blackfan and Harold L. Higgins, Boston, Studies of Amino Acids.

Dr. Henry F. Helmholz, Rochester, Minn., Differential Bactericidal Effects of Various Urinary Antiseptics.

Pan American Conference of Health Directors.—The fourth Pan American Conference of National Directors of Health will be held in Washington, D. C., May 1-8, according to an announcement from Surgeon General (Ret.) Hugh S. Cumming, director of the Pan American Sanitary Bureau. Subjects to be discussed are: serology of syphilis, public health personnel, use of vital statistics from a public health standpoint, preparation of a sanitary code to serve as a model for various countries, preparation of appraisal tests from the point of view of the Americas, housing in rural and urban

districts, mental hygiene, typhoid control, industrial hygiene, undulant fever, poliomyelitis and Chagas' disease. It is expected that about fifty delegates will be present.

Air Lines Complete Year Without an Accident.—Commercial air lines of the United States completed a full year without a fatal accident or serious injury to passenger or crew, it was announced March 27. The last fatal accident took place March 26 at Oklahoma City, it was said. The nineteen domestic air lines flew a total of 87,500,000 miles in the twelve months period. More miles were flown, more planes used, more passengers and mail carried and more scheduled trips completed than in any other year in the history of commercial aviation in the United States. Credit was given to the Civil Aeronautics Authority as well as to the air lines for its insistence on safety precautions.

National Academy of Sciences.—The annual meeting of the National Academy of Sciences will be held in Washington, D. C., April 22-23. Among the speakers will be:

Dr. Aleš Hrdlička, Washington, D. C., Anthropologic Relations Between Siberia and America.
George B. Kistiakowsky, Ph.D., and Richard D. Cramer, A.M., Cambridge, Mass., A Synthesis of Radioactive Lactic Acid.
Drs. George A. Schumacher, Harold G. Wolff and Helen Goodell, New York, Studies in Pain Sensitivity.
Ernest O. Lawrence, Ph.D., Berkeley, Calif., Bombarding Atoms.
Yandell Henderson, Ph.D., New Haven, Conn., The Control of Respiration Under Artificial Respiration.
Louis O. Kunkel, Ph.D., Princeton, N. J., A New Group of Filtrable Saprophytes.
Dr. William G. MacCallum, Baltimore, Viruses and Their Part in Disease.
Harold C. Urey, Ph.D., New York, Chemical Separation of Isotopes.

Academy of Physical Medicine.—The eighteenth annual session of the Academy of Physical Medicine will be held at Richmond, Va., April 24-26, under the presidency of Dr. Harold D. Corbusier, Plainfield, N. J. Hotel headquarters will be the John Marshall and demonstrations and clinics will be held at the Academy of Medicine Building. Brig. Gen. Frank T. Hines, chief, U. S. Veterans' Administration, will be the speaker at the annual banquet. The speakers on the scientific program will include:

Dr. Chevalier L. Jackson, Philadelphia, Mechanical Humidification as a Therapeutic Measure in Acute Respiratory Infections.
Dr. Frederick A. D. Alexander, Albany, N. Y., Nitrogen Inhalation Therapy for Schizophrenia—A Comparison with Other Methods.
Dr. John S. Coulter, Chicago, Physical Medicine in Medical Education.
Howard Carter, B.S., M.E., Chicago, Activities of the Council on Physical Therapy of the American Medical Association.
Milton Harris, Ph.D., Washington, D. C., Studies in the Chemistry of Keratin.
Dr. Gustav Bucky, New York, Problems of Superficial Radiation Therapy.

Medical Stores Bought by Red Cross for War Relief.—Medicines and hospital and surgical supplies loom large in American Red Cross war relief purchases, according to a recent tabulation of articles which that organization is furnishing its sister societies in war-affected countries to assist them in minimizing the sufferings consequent to hostilities. Analysis of the tabulation, dated April 1, reveals the following purchases:

800,000	tablets of sulfanilamide
266,000	tablets of sulfapyridine
100	tons of other assorted drugs
23,000	surgical instruments
38	x-ray units
32	generating motors for x-ray units
1	100 bed hospital unit, containing 700 items
25	hospital tents each of fifty patient capacity
11	motor ambulances
1,500,000	yards of surgical gauze
92,000	pounds of absorbent cotton for medical purposes
276,000	yards of bed sheeting and large quantities of soap, toothbrushes and other similar products

Purchases for relief also included 120,000 blankets, 105,000 suits of knitted underwear, 45,000 pairs of shoes and various other articles of clothing. In addition, women volunteers in Red Cross chapters all over the country have produced 344,000 garments and 500,000 surgical dressings. These are sent to the Red Cross warehouse in New York, where they are packed and shipped to the various Red Cross societies in the nine European countries currently receiving assistance. These are Finland, German-occupied Poland, France, England, Latvia, Lithuania, Rumania, Hungary and Yugoslavia. The latter five countries harbor some 122,000 Polish soldiers and civilians who sought refuge there last September. American Red Cross relief operations in Europe are under the supervision of a commission of two men, James T. Nicholson, from national headquarters, Washington, and Wayne Chatfield-Taylor, former Assistant Secretary of the Treasury. With central offices at Geneva, they are in a position to visit the various relief fronts and personally supervise distribution of supplies and ascertain future needs.

Eighth American Scientific Congress.—As a part of the celebration of the fiftieth anniversary of the founding of the Pan American Union and as a means of advancing scientific thought and achievement in the American republics, the Eighth American Scientific Congress will convene in Washington, D. C., May 10-18, under the auspices of the government of the United States. Included among the eleven sections will be one on public health and medicine, of which Dr. Thomas Parran, surgeon general of the U. S. Public Health Service, is chairman. Subjects on the program have been chosen as follows: nutrition, tuberculosis, cancer, chemotherapy, diseases of the heart, rehabilitation of physically handicapped children, tropical and other diseases. A section on the biological sciences, of which Edwin G. Conklin, Ph.D., emeritus professor of zoology, Princeton University, Princeton, N. J., is chairman, will include in its agenda discussions of general physiology, with emphasis on biochemistry and biophysics, endocrinology, behavior and physiology of whole organisms, and microbiology, including protozoa, bacteria and viruses. Other sections and their chairmen are:

Anthropological sciences, Herbert J. Spinden, Ph.D., curator, division of American Indian Art and Primitive Cultures, Brooklyn Museum, Brooklyn.
Geological sciences, Thomas Wayland Vaughan, LL.D., former director of the Scripps Institute of the University of California.
Agriculture and conservation, Hugh H. Bennett, Sc.D., chief soil conservation service, U. S. Department of Agriculture, Washington, D. C.
Physical and chemical sciences, Lyman J. Briggs, Ph.D., director, National Bureau of Standards, Washington.
Statistics, Stuart A. Rice, Ph.D., professor of sociology and statistics, University of Pennsylvania, Philadelphia.
History and geography, Clarence H. Haring, Ph.D., professor of Latin American history and economics, Harvard University, Cambridge, Mass.
International law, public law and jurisprudence, James Brown Scott, J.U.D., secretary, Carnegie Endowment for International Peace.
Education, Nicholas Murray Butler, Ph.D., president of Columbia University, New York.

President Roosevelt will formally open the congress Friday evening May 10 at the Pan American Union. There will be a trip to Mount Vernon Saturday afternoon and on Sunday a trip to Luray Caverns in Virginia. The first plenary session will be held Monday morning and thereafter section meetings will convene morning and afternoon until the final plenary session Friday afternoon. The delegates will spend Saturday visiting Williamsburg and will go from Washington Sunday May 20 to New York for the Eighth American Scientific Congress Day at the World's Fair. The chairman of the committee organizing the congress is Mr. Sumner Welles, Undersecretary of State; the vice chairman is Warren Kelchner, chief, division of international congresses, Department of State, and the secretary, Alexander Wetmore, Sc.D., assistant secretary of the Smithsonian Institution, Washington. Members of the committee were noted in THE JOURNAL, Dec. 16, 1939, page 2250.

LATIN AMERICA

Personal.—Prof. W. H. Hoffmann of the Finlay Institute, Havana, Cuba, has been elected a member of the Academia Colombiana de Ciencias in Bogotá.

Congress on Tuberculosis.—The Fifth Pan American Congress of Tuberculosis will be held in Buenos Aires and Cordoba, Argentina, October 13-17, under the presidency of Dr. Gumersindo Sayago, Cordoba. The official subjects of discussion will be: evidences of tuberculization of the South American countries, heredity and contagion in tuberculosis, and the pulmonary aspects of the extrathoracic forms of tuberculosis.

CORRECTIONS

Society for Study of Asthma and Allied Conditions.—The Society for Study of Asthma and Allied Conditions will hold its annual meeting in Atlantic City, N. J., May 4 instead of April 29, as announced in the news in THE JOURNAL, April 13, page 1469. The meeting described was that of 1939, a program of which was received recently.

Ludwig's Angina.—In the abstract in the Current Medical Literature department of THE JOURNAL, March 16, page 1021, of Dr. A. C. Williams' paper, entitled "Ludwig's Angina," the sentence beginning in the fourth line from the top of the second column with the words "The tracheotomy incision should commence" is incorrect. Dr. Williams did not describe in his paper the tracheotomy incision but an incision for the drainage of the infected suprahyoid tissues.

Foreign Letters

LONDON

(From Our Regular Correspondent)

March 16, 1940.

Medical Arrangements of British Army in France

The large British army in France cannot yet be said to have engaged in war on any scale. In the severe weather there has been a certain amount of illness, and the arrangements for its treatment have aroused political criticism. Replying to this in the House of Commons Mr. Stanley, the war minister, said that the army had encountered all the difficulties and improvisations which had grown from the sudden and great expansion. When last April it was decided to double the territorial army the medical services were not doubled at the same time. The necessary expansion had taken place since war broke out. The result was that 90 per cent of the medical officers now serving were a few months ago civilian doctors without military training. Another difficulty was accommodation. When a man was seriously ill the only place to treat him was a proper hospital. Instructions were therefore given that in general a man should not be kept in the reception stations for more than forty-eight hours. It was not always easy to find proper accommodation. For tactical or training purposes the troops were distributed all over the country in France, and the accommodation for a post had to be the best that could be found. That unfortunately was sometimes not very good. But it was in connection with the reception stations that most of the criticisms were made. A general review had not shown faulty medical treatment or deficiency of drugs. It had rather shown unsatisfactory conditions of buildings, equipment or attention, which had not endangered the health of the sick but had caused unnecessary hardship. These things were in process of being remedied.

A fair view was that the medical authorities had been faced with great problems due both to the expansion of the army and to the location of the troops in unaccustomed areas for military reasons. But on the whole these difficulties had been tackled with great energy and success. The rate of admission of pneumonia cases had been only slightly higher in January this year than last year, when there was an epidemic, while the mortality was definitely lower. These facts disproved any allegation of inefficiency or carelessness. There had been some sporadic cases of cerebrospinal meningitis. During the last war the mortality was 40 per cent, but under sulfonamide derivatives it had now been reduced to 8 per cent.

Sugar Restrictions and Medicines

As explained in a previous letter, rationing so far has produced only small inconveniences. It is due to the fact that we import a large amount of food the cargo space for which must be limited so as to supply more space for the munitions of war. Sugar is an example of a largely imported food. The ration is 12 ounces a week per person. Its use in the making of preserves also is limited. The Council of the Pharmaceutical Society has been informed that strict economy in the use of sugar for pharmaceutic purposes will be necessary, although the sugar controller has allotted for 1940 for use in the preparation of medicines 100 per cent of the quantity used in 1939. The unusual prevalence of coughs, colds and sore throats during the past winter caused an unprecedented demand for cough mixtures, tinctures and lozenges, which are composed largely of sugar. As a consequence, manufacturers were obliged to make inroads into the supply of sugar intended for the rest of the year. As it is not likely that the allowance will be increased, it will be necessary to eke out what remains. The president of the Pharmaceutical Society is therefore appealing to physicians to prescribe as sparingly as possible medicinal syrups and other preparations containing sugar. He is also appealing to manufacturers and chemists to husband their supplies of sugar. Since the object of using sugar in medicines is to make nasty drugs less unpalatable, it will be no loss to use other sweetening agents. Saccharin or glycerin is suggested as an alternative. Both are produced in this country in a quantity sufficient to stand any strain. A series of formulas for sugar substitutes in medicine is under consideration.

Another result of sugar restriction is that evaporated fruits—apple rings, dried pears, peaches and nectarines—will not be available for the ordinary citizen because the entire supply has been taken by the government for the fighting forces. From the first it was determined that they must not go short whatever may happen to the civilians, who are recommended to take advantage of dried fruits, such as figs, dates and raisins.

PARIS

(From Our Regular Correspondent)

March 6, 1940.

Surgical Ambulances at the War Front

Before a medicosurgical reunion, Merle d'Aubigné reported on the value of the new surgical ambulances during their first weeks of use. Most of the wounds treated were due to bullets and mines. Of these, 14 per cent could be saved by urgent intervention while the rest, inoperable cases or such as could wait, were transferred. The principal difficulties were found to exist in the excision of injured tissues in areas of great vascular and nerve density, in the search of a way of approach in wounds believed to be visceral lesions and in complications encountered in cases of multiple wounds such as those caused by mines. The speaker stressed the need of preparatory care of the wounded, of shock treatment before intervention, of sufficient space and of a trained personnel. It is obvious that surgeons engaged in this service work under precarious conditions.

Refugee Physicians

The doctor's degree in medicine has official significance in France only if conferred on a Frenchman. If it is conferred on a foreigner it is called the university diploma of the medical division and does not grant the right to practice medicine in the French empire. Neither does the title agrégé étranger (university fellow from abroad), given to many distinguished physicians who come to France to undertake research in hospitals and laboratories, allow holding a medical professorship.

However, for a long time the French university degree has been sought by a great many foreigners, either for the honor implied in it or as a step to the state diploma and the practice of medicine. The two diplomas, the university and the state, have come more and more to be in demand. In 1923 French faculties of medicine conferred ninety-six university degrees and 901 state diplomas; in 1933, 170 and 1,293 respectively; in 1938, 257 and 1,394; in 1939, 206 and 1,726. Of 4,072 university degrees conferred on foreigners, 234 were by state diplomas either through naturalization or by authority vested in the state. The recent persecutions of certain national minorities have increased the number of state diplomas of foreigners. Many of these physicians were placed in the French colonies. Some settled in French rural districts deprived of medical services. A large number, however, installed themselves in towns in competition with resident physicians and came in conflict with the syndicate tribunals and even with courts of law. This naturally prejudiced the medical profession against them. The situation is aggravated by another consideration. French physicians don the uniform and join the army; the foreign physician stays behind and takes over their practice. He occupies a privileged position. He can neither serve in the army nor is he subject to civilian requisition. Polish and Czech physicians solved their problem by enlisting in the armies of their nation organized in France,

but many others, such as Rumanian, Syrian and Russian physicians, have no such openings. To meet the situation, the confederation of medical syndicates took active interest in the proposal of a law according to which a foreign physician under 50 years of age would be prohibited under certain conditions to exercise his profession within the radius of 60 to 65 miles from the place where he had been living since the outbreak of hostilities. In addition, naturalization could be refused foreign physicians who abused French hospitality and became guilty of acts contrary to law.

Blood Transfusion

The technic of blood transfusion, the choice between fresh and banked blood and the liquids capable of replacing the blood are current problems. According to Bécart, blood transfusion meets two major indications: hemorrhage and shock. In hemorrhage, lost blood must be replaced; in shock, blood flow retarded in the vascular system needs to be reestablished. However, regularity of movement is lacking at present in all transfusion technics. For that reason Bécart constructed a new apparatus by means of which a regularity analogous to that of natural circulation is effected. He discussed it before the Société de médecine of Paris. The blood flow in this apparatus is continuous and may have sixty, eighty and 100 beats a minute. Like the pulse, its graphic representation is an uninterrupted and regularly positive curve. This rhythm is attained by means of a small pump or, rather, a sort of turbine, the principal factor of which is a cylindric rotor turning always in the same direction, thereby avoiding the shock inflicted on the blood by aspiration and compression. The output is measured by a meter. The bruising of the components of the blood is thus overcome. Reactions which occur at times after transfusion are eliminated. The apparatus is managed either by hand or by a small motor, a colored indicator signifying the frequency of the pulse beats. The simplicity of the mechanism is as remarkable as the conception is ingenious.

Dr. A. Stillmunkes, before the Société de pathologie comparée, opposed the use of blood of dead bodies, subject as it is to dangerous changes. Placental blood, he said, is not always "complete," often presents phenomena of fibrinolysis, is capable of transmitting syphilis and can scarcely be kept for more than forty-eight hours. Safeguards in the refrigeration of the blood of living donors consist in the selection of blood that has preserved its arterial red color. The cells must be intact. If they present indentations, the distinctive intracellular protein substances of the hemoglobin which accumulates about the globule in the form of granulous or filamentous extensions are no longer present. Hemolysis is easy to observe. Stillmunkes used an electric colorimeter with a constant current and a photoelectric cell. Hemolysis appeared about the tenth day whatever the method of conservation employed was, even for fresh blood. All resistance, measured by the classic method of sodium chloride, showed a diminution parallel to that of hemolysis but began somewhat sooner. The conclusion of his researches is that conserved blood can not be used without danger after the seventh day.

Control of Venereal Diseases

War conditions have obliged governments to reinforce prophylactic measures against venereal diseases. On the advice of the recently created Haut comité de la population and of different other agencies engaged in sanitation and moral conditions, the French government has passed some new regulations, several of which had been previously proposed but had evoked popular dissatisfaction as infringing on the liberty of the individual. According to these new measures the physician must point out to the patient the dangers involved and the transmissibility of the disease. Moreover, he must report every case to the health authorities. Information given is of a confidential character. Suspected individuals are required, if requested, to exhibit a medical certificate made out by an approved physician indicating that the bearer is free from the disease. The law can compel infected persons to be treated and to submit to serologic supervision. A training course in syphilology is required of medical students. Restaurant keepers, hairdressers, wine merchants and others are required to employ effective sterilization of equipment and tableware. Drugs sold for the treatment of venereal diseases must conform to approved standards. The effectiveness of the new measures will depend principally on the degree of control exercised by those to whom venereal control has been entrusted.

Sixth Congress of the Therapeutic Union

The sixth annual meeting of the Union thérapeutique was held March 18 in the council chamber of the Faculty of Medicine of Paris. This union was founded in 1934 by Professor Loeper, at that time president of the Société française de thérapeutique. Its purpose is to unite once a year the various therapeutic and pharmacodynamic societies. Thirteen nations were represented, with the minister of public health presiding. In spite of wartime difficulties many foreign delegates put in their appearance, including Burgi of Berne, Rietti of Ferrara, Dustin of Brussels, Marañon of Madrid and numerous delegates of Poland and Czechoslovakia. The first session was devoted to the discussion of phosphorus. Babonneix and Busquet described the treatment of granulocytopenia with nucleotides of pentose and nucleosides. Hazard spoke on the conditions under which phosphates or rather calcium phosphates are absorbed by the intestine, a complex absorption because of the multiple factors governing the metabolism of calcium. Mouriquant and Leulier discussed phosphate deficiency and raised the question of rickets and the relations between phosphorus deficiency and that of vitamins P and D. Dustin reported on physical and leukopoietic medications such as those of arsenic, sulfur and copper, and those of vitamins and glands.

BUENOS AIRES

(From Our Regular Correspondent)

Feb. 27, 1940.

Prize for Medical Novel

The book club of Buenos Aires (Club del Libro) has announced a prize contest for a novel, biography or autobiography dealing with the life, struggles and ideals of a physician and his environment. Historical subjects are also admitted. The background must be exclusively South American. It is open to Spanish-American writers. Manuscripts, not previously published, must be submitted by July 31, 1940. The award will consist of 2,000 Argentine pesos ($595). The club may acquire additional manuscripts at 1,000 pesos ($298). Manuscripts of a political and racial nature are not desired.

A New Insect

A new insect has made its second annual appearance in Buenos Aires, a Coleopterus called Paederus fuscipes brasiliensis. It appears in extremely hot weather, attaches itself to the neck, does not sting and does no harm if removed without crushing. If injured, the beetle exudes an irritant that causes pyrexia and dermatitis. After a few hours the typical picture is that of an erythema and phlyctenae with turbid contents which coalesce and cause extensive tissue destruction, making surgical treatment with drainage necessary.

National Commission for School Aid

It is the purpose of the Argentine government to maintain throughout the country a vigorous policy of social aid for school children, in accordance with resolutions of the Argentine parliament. As a first step 594 school lunch arrangements were recently organized and garments distributed that affected 74,000 children. The federal government has appropriated 2

million Argentine pesos ($595,000) and founded the national commission for school aid, which is charged with the responsibility of expeditiously carrying out the measures adopted by the government. The commission consists of government and school officials in leading positions and of the president of the federal public health service.

Feeding School Children in Chile

The minister of health, in cooperation with the bureau of nutrition, has instituted school breakfasts, consisting of milk chocolate and bread, in Chile. It is estimated that 400,000 Chilean children need a school breakfast. This will require an appropriation of 18 million Chilean pesos ($5,358,600). A further difficulty in carrying out this project lies in the comparative scarcity of milk.

Noxious Gases

The health department of Buenos Aires has made investigations to determine to what extent the consumption of fuel oil used by motor busses is a public nuisance. These black, thick gases are extremely unpleasant and also prejudicial to health. Motor busses using this oil are, therefore, required to attach contrivances to counteract these noxious effects. Public opinion demands the suppression of motor fumes within the city.

Congress of Surgeons

Early in January the second congress of South American surgeons was held in Santiago de Chile, at which delegates from Uruguay, Peru, Bolivia, Paraguay and especially Argentina were present. The first scientific session was devoted to the discussion of the physiopathology and treatment of goiter. Dr. José Caciro of Argentina, Dr. V. Pérez Fontana of Uruguay and Dr. E. Betermann of Chile led the discussions. The subject of the second day was vertebral fractures, with Drs. E. Lagomarsino of Argentina, L. Bado of Uruguay and I. Horvitz of Chile speakers. Dr. Manuel L. Pérez of Buenos Aires read a paper on puerperal peritonitis, the third subject.

Endemic Goiter in Argentina

Endemic goiter, known in Argentina since the time of the Spanish conquest, is definitely traceable to iodine deficiency in water, soil and foods of certain regions. For that reason potassium iodide has been furnished free of charge since 1924, in tablets of from 0.005 to 0.01 Gm., by the public health service to the indigent. The greatest incidence of goiter is in several northern provinces (Salta, Tucumán and Jujuy) and in the Andes region. In one of these northern valleys 83 per cent of the school children were afflicted; the general incidence in these northern provinces fluctuates between 50 and 75 per cent. The plain sections of the country, with a few exceptions, are free from goiter. The most common form of goiter that prevails is of the type that is scarcely visible.

Spanish-American Hospital Congress

The first Spanish-American hospital congress was held January 7-13 in Santiago de Chile and in Valparaiso. Official delegates of Argentina, Colombia, Venezuela, Paraguay, Panama, Guatemala, Bolivia, Uruguay, Ecuador, Peru and the Dominican Republic participated. Concurrently, hospital exhibits were held and courses on hospital management given. It was pointed out that European hospital systems could not be transferred to Spanish-American conditions without adaptations. A resolution was passed requesting Spanish-American university bodies to promote the science of nutrition by special courses and to create standards for the preparation of special diets. During the congress a sanatorium was dedicated in Valparaiso, built at the cost of 8 million Chilean pesos. Recommendations were made that South American governments organize hospital associations to meet at regular intervals for the exchange of administrative and scientific points of view. The creation of a periodical for hospitals was likewise recommended. Great improvements for hospital management are expected from the extensive deliberations of these meetings. The next session is to be held in Bogotá, Colombia.

Control of Venereal Diseases in Argentina

The national public health service has issued a report on the control of venereal diseases achieved since the law governing venereal prophylaxis went into effect in June 1937. By centralizing all service bureaus under unified control, the law made possible the observation and treatment of all persons with venereal afflictions. It provides free hospital treatment and requires obligatory treatment of infectious cases, compulsory hospitalization of those resisting treatment, individual prophylaxis, premarital certificates for men, regulation of prostitution and the suppression of brothels. In general, all hospitals in Argentina except those for tuberculosis, leprosy and mental diseases have a division or a consulting bureau for the treatment of venereal diseases. There are about 570 centers.

The national public health service has an abundance of drugs, especially arsphenamine; at the same time the manufacture of bismuth and mercury preparations was intensified. The method used is the mixed intermittent therapy recommended by the League of Nations but more intensive in the total amount of the drug taken and continuing for a longer time. In the first year, three series of neoarsphenamine totaling 21 Gm. are administered and three series of bismuth compounds of respectively twenty, eighteen and sixteen injections, every two weeks. In the first two series neoarsphenamine and bismuth compounds are given simultaneously; in the third, neoarsphenamine alone; in the fourth, bismuth compounds alone. An interval of four weeks occurs between the treatments. The follow-up period lasts three years, in which respectively four, three and two series with bismuth are conducted, each of sixteen injections. In the antivenereal wards and consulting bureaus in Buenos Aires a marked recession of new cases of syphilis has been noted since 1934. A marked reduction during the same period has also been observed for cases of chancroid, which is treated with Nicolle's vaccine. Nothing definite can yet be said regarding venereal lymphogranuloma.

To facilitate diagnosis, the national public health service has organized six bacteriologic diagnostic centers in the larger cities in addition to the bacteriologic institute in Buenos Aires. Specimens to be examined can reach one of these centers within twenty-four hours. The public health service is authorized by law to supervise all private diagnostic institutes. Training courses are also planned in Buenos Aires for physicians in charge of antivenereal control.

The certificate required of all men before marriage is issued by certain physicians (1,800 out of 11,700) who exercise official or hospital functions or are given special authority by the public health service. The enforcement of the prenuptial examinations has not encountered the difficulties expected or reduced the number of marriages. A museum is being organized in Buenos Aires to aid venereal control by means of lectures, films, demonstrations and printed information.

Specific drugs used in venereal control can be imported without payment of a tax. Drugs are furnished only on medical prescription, to avoid quackery. Advertisements in the daily papers are also under the jurisdiction of the national public health service. In 1937, 40,847 recruits showed a 1.66 per cent incidence of venereal disease; in 1938 it fell to 0.87 per cent in 42,231 men. A similar reduction was noted in soldiers the first half year of military service: 2.43 per cent in 1937 against 0.95 per cent in 1938.

Personals

Dr. Aníbal Ruíz Moreno, president of the Argentina League against Rheumatism, is on his way to the United States to study the organization of rheumatism control. His investigations are sponsored by the faculty of medicine of Buenos Aires.

According to an announcement made by Prof. A. H. Roffo, Argentine cancer expert in Buenos Aires, the University of Wisconsin Medical School has created a fellowship valued at 10,000 Argentine pesos ($2,977) annually in the institute of experimental medicine. The purpose of the fellowship is to create a closer cooperation between the research institute of Buenos Aires and the newly created institute of the University of Wisconsin.

In Paris there exists the Fondation Angel Roffo, which seeks to promote scientific relations between France and Argentina by fellowship grants. The French League against Cancer, entrusted with the award of these fellowships, has made available 25,000 francs ($530) for the appointment in 1940 of a Frenchman for research work at the institute directed by Professor Roffo in Buenos Aires.

G. Bosco, professor of symptomatology in Buenos Aires, was awarded the Bourceret prize by the Academy of Medicine in Paris for his "Anatomotopographic Diagnosis of the Occlusion of the Coronary Artery."

Prof. Oscar Orias was appointed professor of physiology and director of the physiologic institute of the Faculty of Medicine at the University of Córdoba.

The Sociedad Argentina de psicoanálisis was founded as an affiliate of the Asociación Médica Argentina January 12. Prof. Juan Ramón Beltrán, professor of the history of medicine, was elected president.

Dr. José A. Pérez, associate professor at the University of Córdoba and director of a hospital, was given leave by the university to continue research studies, principally on tuberculosis, in the United States, at the State Health Department of New York, the Henry Phipps Institute in Philadelphia and the National Institute of Tuberculosis in Minneapolis.

A society for the study of allergy has been organized in Buenos Aires. Last year the Academy of Medicine in Buenos Aires arranged a series of lectures on allergy.

ITALY

(From Our Regular Correspondent)

Feb. 29, 1940.

National Congress of Urology

The eighteenth national congress of the Società Italiana di Urologia was held recently at Naples. The first official topic concerned traumatology and industrial accidents of the urinary tract, with Professors De Gironcoli of Treviso and Nisio of Bari the official speakers. De Gironcoli discussed the lesions of the bladder and the urethra. In the war in Spain the largest number of ruptures of the deep urethra was due to automobile accidents. The speaker believes that the ultimate results of the treatment depend on the opportunity of an early operation rather than on the seriousness of the lesion and the presence of complications.

Professor Nisio discussed trauma of the kidneys and ureters in industrial accidents. He believes that, in evaluating the effects of accidents in relation to compensation, one must consider the general condition of the worker before the accident, as there may be physiologic or pathologic conditions which may act as causes in the evolution of the traumatic lesions. An interesting problem is the evaluation of working capacity when one kidney is lost and the remaining one is normal. The tables of insurance institutions for workers show an estimation of 25 per cent diminished working capacity. The author believes that the working capacity is diminished 40 per cent when one kidney is lost.

Dr. Sorrentino made a statistical report covering more than 80,000 cases of trauma observed in the Naples Hospital, among which were 246 cases of renal trauma. Professor Tarallì discussed medicolegal evaluation of working capacity in trauma on the urinary tract. He believes that an estimate of 25 per cent reduction of working capacity after nephrectomy in the presence of a normal remaining kidney is fair.

The second official topic was on disturbances of the bladder in relation to functional and organic alterations of the nervous system. Professors Sacco and Caporale of the Genoa and Turin universities, respectively, were speakers. Caporale discussed disturbances of micturition due to lesions in the brain, spinal cord and peripheral nervous system. In the presence of lesions of the brain, the disorder of the bladder does not call for direct treatment. It subsides as the nervous condition improves from proper treatment. Cystometry in association with other methods for the diagnosis of urologic disorders is important in the diagnosis of the nervous disease, as the functions of the sympathetic, parasympathetic and voluntary factors in the physiology of micturition can be separately determined.

Personals

Prof. Ludovico Tommasi has been appointed head of the clinica dermosifilopatica of the University of Naples. He was appointed to the chair of clinical medicine in the University of Sassari in 1925 and later on to the Palermo University. He has published many articles. He was president of the Società Italiana di Dermatologia e Sifilografia for four years.

Prof. Luigi Auricchio, head of the clinica pediatrica of Naples, was recently appointed head of the university, from which institution he graduated in 1920.

Prof. Mario Mazzeo was appointed to the chair of hygiene of the University of Naples to fill the position left by Dr. De Blasi, who was transferred to Rome. He has written more than 100 articles on microbiology, immunology, social hygiene, the resistance of Brucella to disinfectants, immunization reactions of animals subjected to various treatments, frequency of tuberculosis in bakers, relation between epinephrine and cholesterol, and the effect of disturbances of these substances in the evolution of infections.

Deaths

G. G. Perrando, professor emeritus in legal medicine and in insurance medicine in the Genoa university, is dead. He wrote a manual on legal medicine.

Prof. Aristide Busi, a senator, head of the Istituto di Radiologia Medica of the University of Rome, former president of the Facoltà di Medicina of Rome, founder fellow and president of the Società Italiana di Radiologia Medica, died in Rome. He was the organizer of two large institutions for radiologic work. He wrote a book on x-ray diagnosis.

Marriages

JOSEPH M. HUERKAMP, Fort Recovery, Ohio, to Gene Emerson Swearingen at Portland, Ind., in February.

JULIAN J. FERTITTA, Beaumont, Texas, to Miss Elizabeth Bassett Hayward of New Orleans in February.

OTIS WAYNE YEAGER, Rockmart, Ga., to Miss Julia Lee Bowman at Birmingham, Ala., February 24.

HERMAN G. RUBIN, Akron, Ohio, to Miss Eileen Strauss of Sumter, S. C., in Chicago, February 25.

WILLIAM F. CARTER to Miss Bess Salmon, both of Pleasureville, Ky., in Eminence, March 15.

JACOB EDWARD HERSHBERGER, Dayton, Ohio, to Miss Louise Koester of Toledo in February.

JOHN T. CATER to Miss Jessie Ervin Howell, both of Montgomery, Ala., March 23.

DANIEL G. CAUDY, Zanesville, Ohio, to Miss Ann Saum of Dayton, Dec. 24, 1939.

KEITH J. LONG, Fairview, Ill., to Miss Dorothy Wood of Peoria, February 7.

ISADOR BLUM, New York, to Miss Ruth Klar of Elizabeth, N. J., March 21.

Deaths

Bernard Fantus ● distinguished as a leader in the field of therapy, died of myocarditis at the age of 65 at his home in Chicago, April 14.

He was born in Budapest, Hungary, Sept. 1, 1874. After preliminary study in Vienna he came to the United States, where he attended the University of Illinois School of Medicine and received his M.D. degree in 1899. He did graduate study in pharmacology at Strasbourg in 1906, at Berlin in 1909 and at the University of Michigan in 1917, from which he received the degree of master of science. He served as associate attending physician at the Cook County Hospital 1901-1902 and was in charge of the medical dispensary at the University of Illinois 1902-1913. From 1903 to 1924 he was professor of pharmacology and therapeutics at the University of Illinois School of Medicine and then taught as associate professor of medicine at Rush Medical College from 1924 to 1932. Since 1932 he had been professor of pharmacology, materia medica and therapeutics at the University of Illinois. He served also as professor of physiology at the College of Pharmacy of the University of Illinois from 1913 to 1917. Since 1930 he had been attending physician to the University Hospital and since 1934 director of therapeutics at the Cook County Hospital.

Dr. Fantus contributed widely to scientific medical literature and conducted numerous original investigations in the field of therapy. His research covered particularly such topics as the use of candy medication, the technic of medication and, more recently, the preservation of blood. In 1933 he was awarded the first honorary degree given by the American Therapeutic Society for his work in making medication more palatable for children. The "blood bank" at the Cook County Hospital was established by him on March 15, 1937, and his plan of organization has been widely followed. Since 1918 he had been editor of the "Year Book of General Therapeutics." His contributions to medical literature include also "Prescription Writing," "Candy Medication," "Useful Cathartics" and "Technic of Medication" and many periodical articles.

For many years he contributed his time and his efforts toward the establishment of an area in Chicago surrounding the Cook County Hospital and the nearby medical schools and hospitals as a medical park. More recently he was chairman of the Committee on Spas of the American Medical Association. He was an indefatigable worker, a genial personality and an inspirational contributor in the field of therapeutics.

John Andrew Amyot, Ottawa, Ont., Canada; University of Toronto Faculty of Medicine, Toronto, 1891; at one time professor of hygiene at his alma mater; established the first postgraduate course at the University of Toronto, leading to the D.P.H. qualification; established and directed the Provincial Laboratory of Ontario; was the first deputy minister of the newly organized federal department of health, later deputy minister of the department of pensions and national health, and deputy minister of health; represented Canada on several occasions in the health section of the League of Nations; served with the Canadian Army during the World War; aged 72; died, February 13.

Samuel Clark Red ● Houston, Texas; Jefferson Medical College of Philadelphia, 1887; fellow of the American College of Surgeons; member of the House of Delegates of the American Medical Association in 1929; past president of the Harris County Medical Society and the State Medical Association of Texas; for many years president of the school board; member of the staff of St. Joseph's Infirmary; aged 78; died, February 25.

Kenneth Mercereau Davenport ● Watertown, N. Y.; University of Michigan Medical School, Ann Arbor, 1927; formerly a passed assistant surgeon in the U. S. Public Health Service reserve; member of the American Academy of Dermatology and Syphilology; aged 38; died, February 15, of burns received when he attempted to rescue his family from a burning building.

Roy Stanley Smith, Detroit; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1914; member of the Michigan State Medical Society; on the staffs of the Mount Carmel Mercy Hospital, St. Joseph's Mercy Hospital and the Highland Park General Hospital; aged 52; died, February 29, in St. Petersburg, Fla., of coronary thrombosis following hemorrhoid ligation.

George Alfonzo Peirce, Enfield, N. H.; Harvard Medical School, Boston, 1898; member of the Massachusetts Medical Society and the New England Society of Psychiatry; served during the World War; formerly assistant superintendent of the Tewksbury (Mass.) State Hospital and Infirmary; aged 65; died, February 21, of cirrhosis of the liver and arteriosclerosis.

Frank Ott Stem, Berlin, N. J.; Jefferson Medical College of Philadelphia, 1891; bank president; mayor; formerly county physician and coroner; medical director of the Camden County General Hospital and the Camden County Hospital for Mental Diseases, Grenloch; aged 70; died, February 6, of respiratory infection, cardiac decompensation and renal insufficiency.

Moses Emmett Blahd, Cleveland; Western Reserve University Medical Department, Cleveland, 1906; member of the Ohio State Medical Association; fellow of the American College of Surgeons; served during the World War; on the staff of the Mount Sinai Hospital; aged 56; died, February 28, in Tucson, Ariz., of carcinoma of the rectum and liver.

George James Alexander, Bala-Cynwyd, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1905; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; aged 64; died, February 24, in the Philadelphia General Hospital of arteriosclerosis.

Carroll Burton Bacon ● Waterloo, N. Y.; Jefferson Medical College of Philadelphia, 1896; for many years president of the board of education, and county coroner; served at various times as health officer; on the staff of the Waterloo Memorial Hospital; aged 71; died, February 24, of carcinoma of the prostate.

Edwin Joseph Kehoe, San Francisco; Miami Medical College, Cincinnati, 1903; at one time superintendent and medical director of the county tuberculosis sanatorium, Pontiac, Ill.; for many years associated with the U. S. Veterans' Bureau; aged 65; died, February 12, in the Stanford University Hospital.

Allan Marshall Wilkinson ● Los Angeles; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1901; served during the World War; on the staffs of the Children's Hospital, Hollywood Hospital and the California Hospital; aged 64; died, February 1, of influenza and pneumonia.

Juanita McFarland Jennings, Louisville, Ky.; Lincoln Memorial University Medical Department, Knoxville, Tenn., 1911; member of the Kentucky State Medical Association; field director in the division of county health, state board of health; aged 51; died, February 24, of carcinoma of the lung.

Benjamin Leon Grodnitzky, Saratoga Springs, N.Y.; University of St. Vladimir Faculty of Medicine, Kiev, Russia, 1899; Université de Paris Faculté de Médecine, France, 1930; on the staff of the Saratoga Hospital; aged 66; died, February 24, at Boston of embolism following an operation.

William Jackson Melvin, Darke, W. Va.; Kentucky School of Medicine, Louisville, 1890; member of the West Virginia State Medical Association; member of the board of county commissioners; aged 72; died, February 19, in the Charles Town (W. Va.) Hospital of pneumonia.

Thomas Joseph Toner, Wentzville, Mo.; Northwestern University Medical School, Chicago, 1906; member of the Missouri State Medical Association; served during the World War; aged 64; died, February 22, in St. Joseph's Hospital, St. Charles, of aneurysm of the aorta.

Louis Edward Printy, St. Louis; St. Louis University School of Medicine, 1911; senior instructor in internal medicine at his alma mater; assistant physician to St. Mary's Group of Hospitals; served during the World War; aged 51; died, February 18, in the Desloge Hospital.

Lemuel A. Templeton, Huntland, Tenn.; Vanderbilt University School of Medicine, Nashville, 1889; University of Nashville (Tenn.) Medical Department, 1902; aged 76; died, January 11, in the Lincoln County Hospital, Fayetteville, of carcinoma of the prostate.

Louis William Scherman, St. Louis; Homeopathic Medical College of Missouri, St. Louis, 1900; member of the Missouri State Medical Association; on the staffs of the Deaconess Hospital and St. Anthony's Hospital; aged 61; died, February 20, of coronary thrombosis.

Daniel Blake Harris, Munford, Ala.; Southern Medical College, Atlanta, 1897; member of the Medical Association of the State of Alabama; for many years member of the county board of education; aged 67; died in February at the Citizens' Hospital, Talladega.

Robert Bruce Cameron, Defiance, Ohio; Starling Medical College, Columbus, 1873; member of the Ohio State Medical Association; formerly member of the state legislature; at one time county health officer; aged 94; died, February 22, of coronary occlusion.

Taswell Pittman Haney Sr., Iuka, Miss.; Memphis (Tenn.) Hospital Medical College, 1907; member of the Mississippi State Medical Association; county health officer; aged 72; died, February 22, in the McRea Hospital, Corinth, of coronary thrombosis.

Henry Francis Cassidy, Baltimore; University of Maryland School of Medicine, Baltimore, 1890; member of the Medical and Chirurgical Faculty of Maryland; for many years police physician; aged 70; died, February 12, in Roland Park, Md.

Charles Arthur Thompson, Newton, Mass.; College of Physicians and Surgeons, Baltimore, 1896; member of the Massachusetts Medical Society; aged 67; died, February 3, in the Newton Hospital of cerebral hemorrhage and arteriosclerosis.

Thomas Edmond Benton, Lonoke, Ark.; Memphis (Tenn.) Hospital Medical College, 1901; formerly coroner and city health officer; aged 64; died, February 5, in a hospital at Little Rock of bronchopneumonia and cerebral arteriosclerosis.

Fletcher Bliss Forrest, Bellwood, Pa.; Southern Homeopathic Medical College, Baltimore, 1904; member of the Medical Society of the State of Pennsylvania; aged 62; died, February 8, in the Altoona (Pa.) Hospital of a streptococcic septicemia.

James V. Beghtol, Hastings, Neb.; College of Physicians and Surgeons, Keokuk, Iowa, 1877; member of the Nebraska State Medical Association; aged 88; died, February 6, in the Mary Lanning Memorial Hospital of cerebral hemorrhage.

Albert Wilberforce Williams, Chicago; Northwestern University Medical School, Chicago, 1894; member of the Illinois State Medical Society; on the staff of the Provident Hospital; aged 78; died, February 26, of coronary thrombosis.

De Witt Farmer Morgan ● Okolona, Miss.; Tulane University of Louisiana School of Medicine, New Orleans, 1899; at one time county health officer; at one time bank president; aged 71; died, February 17, of coronary thrombosis.

William Gardiner Symon, ● Garrett, Ind.; University of Colorado School of Medicine, Denver, 1913; member of the American Academy of Ophthalmology and Otolaryngology; aged 54; died, February 28, of heart disease.

Robert Reagles, Arlington, Wis.; Rush Medical College, Chicago, 1894; aged 78; died, February 3, in Madison (Wis.) General Hospital of bronchopneumonia, cerebral thrombosis, arteriosclerosis and chronic myocarditis.

Frank Devlin, ● Newark, N. J.; Long Island College Hospital, Brooklyn, 1897; aged 72; on the staff of City Hospital and St. James Hospital, where he died, February 23, of injuries received in an automobile accident.

Charles E. Hurley, Bentonville, Ark.; Arkansas Industrial University Medical Department, Little Rock, 1892; member of the Arkansas Medical Society; aged 72; died, February 29, of encephalitis and encephalomalacia.

Robert Emmett Eagan, Long Beach, Calif.; Louisville (Ky.) Medical College, 1896; member of the Kansas Medical Society; aged 69; died, February 1, of cerebral hemorrhage, hypertension and arteriosclerosis.

Samuel Jones Bampfield, Denmar, W. Va.; Howard University College of Medicine, Washington, D. C., 1904; superintendent of the Denmar Sanitarium; aged 62; died, February 22, of cerebral hemorrhage.

Noah Franklin Turner, Birmingham, Ala.; Meharry Medical College, Nashville, Tenn., 1906; aged 62; was killed, February 17, when the automobile in which he was driving was struck by a train.

Robert Cartwright Cheney ● Boston; Harvard Medical School, Boston, 1919; member of the New England Ophthalmological Society; aged 45; died, February 8, of a self-inflicted gunshot wound.

Joseph Roderick Winnett ● Eldora, Iowa; Drake University College of Medicine, Des Moines, 1912; served during the World War; aged 53; died, February 8, of metastatic carcinoma of the spine.

William Bolander Hall, Boise City, Okla. (licensed in Oklahoma under the Act of 1908); county health superintendent for many years; aged 86; died, January 11, of cerebral hemorrhage.

John William Craig, Many, La.; Louisville (Ky.) Medical College, 1884; member of the Louisiana State Medical Society; aged 80; died, February 12, in the Highland Sanitarium, Shreveport.

David W. Levy, Philadelphia; Medico-Chirurgical College of Philadelphia, 1889; member of the Medical Society of the State of Pennsylvania; aged 82; died, February 11, of bronchopneumonia.

Harry Martin Gangloff, Pittsburgh; Cleveland Homeopathic Medical College, 1907; served during the World War; aged 60; died, February 3, of arteriosclerosis and coronary occlusion.

Henry J. Whitney, Olympia, Wash.; California Medical College, Oakland, 1883; University of Oregon Medical School, Portland, 1888; Civil War veteran; aged 92; died, February 6, in Retsil.

Homer P. Yeater, Cole Camp, Mo.; Ensworth Medical College, St. Joseph, Mo., 1892; aged 71; died, February 1, in the Research Hospital, Kansas City, of hypertrophy of the prostate.

Norris Stanley McDowell ● Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1895; aged 66; died, February 8, of lymphosarcoma and rupture of the spleen.

Leon C. Ives ● Peoria, Ill.; Chicago College of Medicine and Surgery, 1916; served during the World War; aged 49; died, February 29, in the Proctor Hospital of gastric carcinoma.

Edward Kingsbury Ross, New York; Columbia University College of Physicians and Surgeons, New York, 1904; aged 69; died, February 21, in the Wyckoff Heights Hospital, Brooklyn.

Edward O. McDermott, Wilmot, Ark.; University of Louisville (Ky.) Medical Department, 1887; aged 74; died, February 13, of abscess of the lung following influenza.

Jesse Benton Titterington, Dallas, Texas; Bellevue Hospital Medical College, New York, 1897; aged 71; died, February 18, in St. Paul's Hospital of cirrhosis of the liver.

Orman Brown Humphrey, Bangor, Maine; Dartmouth Medical School, Hanover, N. H., 1894; aged 72; died, February 24, in Coral Gables, Fla., of coronary thrombosis.

Charles A. Goudchaux, Big Cane, La.; University of the South Medical Department, Sewanee, Tenn., 1897; aged 69; died, January 27, of acute dilatation of the heart.

Luther H. Burnett, Kansas City, Mo.; State University of Iowa College of Medicine, Iowa City, 1878; formerly a druggist; aged 84; died, February 22, in St. Mary's Hospital.

Ernest A. Downey, Huntland, Tenn.; Memphis (Tenn.) Hospital Medical College, 1910; aged 56; died, February 18, in the Lincoln County Hospital, Fayetteville.

Willis H. Keenan, Coshocton, Ohio; Ohio Medical University, Columbus, 1905; served during the World War; aged 61; died, February 28, of cerebral hemorrhage.

Leon Bowman, New York; Columbia University College of Physicians and Surgeons, New York, 1896; aged 66; died, February 11, of coronary thrombosis.

John Thomas Patton, New Weston, Ohio; Starling Medical College, Columbus, 1897; aged 74; died, February 26, at the Miami Valley Hospital, Dayton.

Jose S. Arrache Battistini ● Yauco, P. R.; College of Physicians and Surgeons, Baltimore, 1915; aged 45; died, January 21, of a self-inflicted wound.

John Washington St. Sing, Kellyville, Okla.; University of Nashville (Tenn.) Medical Department, 1909; aged 61; died, February 3, in a hospital at Tulsa.

Edward Blake Richardson, Orleans, Mass.; Boston University School of Medicine, 1891; aged 72; died, January 22, of carcinoma of the intestine.

Bruce Flagg Daniels, McGraw, N. Y.; Boston University School of Medicine, 1934; aged 32; died, February 13, of a gunshot wound, self inflicted.

John B. Atchley, Lebanon, Mo.; American Medical College, St. Louis, 1882; aged 85; died, February 25, in St. Vincent's Hospital, Little Rock.

Horace W. Reid, Oakland City, Ind.; Physio-Medical Institute, Cincinnati, 1881; aged 88; died, February 27, of myocarditis and influenza.

Caleb C. Cochran, Nashville, Tenn.; College of Physicians and Surgeons, Keokuk, Iowa, 1897; aged 93; died, February 26, of senility.

Paul Andrew Lawrence, Mooringsport, La.; Memphis (Tenn.) Hospital Medical College, 1900; aged 68; died in February.

Marvel Thomas, Gillespie, Ill.; Missouri Medical College, St. Louis, 1884; aged 84; died, February 16, of cerebral hemorrhage.

Bureau of Investigation

SOME ALLEGED "DELAYED PERIOD" CURES

The Fraudulent Nostrums of Isidore Hymes Debarred from the Mails

A fraudulent medical mail-order business conducted under various names from Lowell, Massachusetts, was debarred from the mails July 21, 1939. Most of the material that follows is based on data given by the Solicitor for the Post Office Department in a memorandum to the Postmaster General recommending the issuance of a fraud order.

In 1918, according to the report, one Isidore Hymes incorporated at Lowell a business known as Western Refining Company, with a capital of $20,000. Hymes owns 99 per cent of the stock and the other 1 per cent is owned by his family. One of the assets of the business is a drug store from which Hymes conducted his mail-order business under various trade names. Some of these were:

Cote Products Company, 205 Middlesex St., Lowell.
The Motex Company, 16 Robeson St., Lowell.
Florence Richmond.
Betty Lakin.

The business of these variously named concerns consisted in selling through the mails certain pills and capsules for the alleged relief of "delayed menstruation." The products were designated:

Cote No. 1 Pills ($2 a box of 20 pills)
Cote Special Formula 4XXXX ($3 a box)
Cote Super-F Capsules ($5 a box)
Regular Motex Pills ($2 a box)
Special-X Motex Pills ($3 a box)
Motex Super-F Capsules ($5 a box)

It is notorious that "patent medicines" sold for the alleged relief of what is euphemistically called "suppressed menstruation" are most frequently bought by women who, believing themselves pregnant, wish to produce an abortion. It is usual for those who sell products of this type to offer them in what are alleged to be varying "strengths," the so-called stronger pills being sold at much higher prices. For the sellers know that women will buy the higher priced pills or potions in the hope of producing the effect desired. In this respect the business of Isidore Hymes was conducted along orthodox lines. It also ran true to type in that none of the advertisements frankly stated that the pills or capsules would produce an abortion. To have so admitted would have been to violate a federal law.

But neither did the advertising come out frankly in easily understood language and warn purchasers that the Cote or Motex pills or capsules were not sold for abortifacient purposes. What Mr. Hymes's concern did say, under paragraphs headed "The Ethical Purpose of Cote [or Motex] Pills," was that the pills could "not produce return of regularity when same is impossible"—a statement of fact self evident to the point of futility. The same paragraphs also specified that in cases in which "the female organs have been removed" by surgical operation the Cote or Motex pills could not produce menstruation—another obvious truism. Nor, the advertising continued, could they "be effective if change of life has been passed" nor "where the delay is caused by systemic disease, or by ulceration of the womb or a gravid condition of same." This last was presumably included as an attempt to avoid being charged with recommending the products for abortifacient purposes.

But how many women of the type that buy nostrums of this sort know that the expression "a gravid condition" of the womb means pregnancy?

The composition of the Hymes nostrums was similar to that of most of the abortifacient "patent medicines." They contained varying amounts of such irritant volatile oils as green apiol and oil of savin; they contained such purgatives as aloes and castor oil; they also had extract of cotton root bark, oil of rue, "ergotin (Bonjean)" and so on.

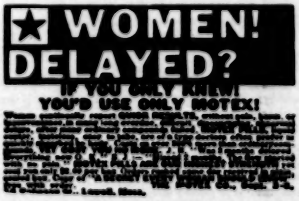
When the concerns were notified to show cause why a fraud order should not be issued against them their attorneys filed a motion to suspend the proceedings on the ground that another governmental agency was considering action against the outfit. This doubtless referred to the fact that the Federal Trade Commission had issued a complaint against the Western Refining Company, Inc., trading as The Motex Company and Cote Products Company, charging that the companies' representations that their products were "safe, competent and reliable remedies" were, in fact, false and misleading.

The Post Office Department's answer to the attorneys was that the "other governmental agency" was suspending action pending final disposition of the case by the fraud order department of the Post Office; hence the motion to suspend was denied. A hearing was held in June 1939 and lasted about two days. In behalf of the government there appeared Dr. Robert E. Herwick, who, as a pharmacologist and toxicologist, testified that the amount of apiol in the nostrums might prove poisonous to the users. In this connection it is worth noting that Sollmann[1] in discussing apiol and savin states that, as regards the former, "Fatal poisoning, with intestinal symptoms, icterus and uremia, is reported," while in the case of the latter "Poisoning has often occurred from their use as abortifacients." Sollmann also remarks, in discussing intestinal irritants used for abortifacient purposes:

> "It must be remembered that these irritants produce their ecbolic effect only secondarily to a gastro-enteritis. The latter may be so violent as to be fatal without accomplishing the desired [abortifacient] result."

Another physician who appeared for the government was Dr. Herman Hertzberg, also of Washington, who testified as a specialist in the fields of gynecology and obstetrics. His testimony was to the effect that the various preparations under discussion were ineffective in the treatment of the several causative and accompanying conditions of amenorrhea and dysmenorrhea.

Hymes's attorneys are reported to have offered no medical testimony of any nature in support of their case. As a result the Solicitor for the Post Office Department, Judge Vincent M. Miles, recommended the issuance of a fraud order against the variously named companies and their officers and agents as such.



A typical Motex Co. advertisement.

In closing it is worth putting into the record the fact that this was not the first time that Hymes ran afoul of the fraud order department of the Post Office. In 1933 he was selling through the mails a preparation for the alleged restoration of "lost manhood" as well as a treatment "for the restoration of the menstrual flow delayed on account of pregnancy." When the postal authorities were about to issue a fraud order in this earlier case, Hymes executed an affidavit agreeing to discontinue his scheme. Hymes's lawyers made a similar attempt in the present case—an informal offer to the government to stipulate the discontinuance of the present scheme and thus avoid a fraud order issuance—but the Post Office authorities refused to accept the offer.

The Federal Trade Commission, on following up the complaint referred to at the top of this column, reported on April 6, 1940, that it had issued an order prohibiting the Western Refining Company, Lowell, Mass., also trading as The Motex Company and Cote Products Company, from making certain misrepresentations in the sale of Motex, Motex Pills and Cote Pills. Among these were that the products constitute safe, competent or scientific remedies for delayed menstruation, contain no harmful or dangerous drugs, and will have no ill effects on the body.

1. Sollmann, Torald: A Manual of Pharmacology, Philadelphia, W. B. Saunders Company.

Correspondence

MEETING OF INTERNATIONAL LEAGUE AGAINST RHEUMATISM

To the Editor:—We wish to correct an impression which seems to exist that the Ligue internationale contre le rheumatisme, which was to hold its seventh congress in America in the early part of the summer of 1940, has been permanently dissolved. The president of the league, Dr. Ralph Pemberton, and the chairman of the American committee of the league, Dr. Robert B. Osgood, feel that this is an entirely erroneous impression. The activities of the league have been temporarily suspended for the duration of the war, but we fully expect to hold the next congress of the league in America as soon after the war as such a congress would seem likely to be successful. Both the British and the American sentiment strongly favor the resumption of the league activities as soon as this is possible.

LORING T. SWAIM, M.D., Boston.
Secretary, American Committee of the Ligue internationale contre le rheumatisme.

GRADING MILK IN NEW YORK CITY

To the Editor:—A letter printed in the March 2 issue (page 821) of THE JOURNAL and signed by Dr. I. Newton Kugelmass on the topic of "Grade A vs. Grade B milk in New York City" prompts the following statement intended to clarify the position of the New York City Department of Health with regard to the grading of milk in our city:

The department has had this matter under consideration for some time, feeling that the reasons for the adoption of milk grading in this city in 1911, when five different grades were established, no longer prevail today. At that time methods of milk production on farms, transportation and refrigeration facilities were somewhat primitive compared to those in operation today, and there was little commercial pasteurization of milk. The quality and the safety of the general milk supply were so questionable that it was necessary to grade milk according to its fitness for infants (grade A pasteurized), for adults (grade B pasteurized) and for cooking (grade C) in addition to "certified" and "grade A raw" milks.

Progressive advances in the sanitation and processing of milk during recent years have greatly improved the quality of the milk supply. With the advent of pasteurization of all milk, except certified, two of the original five grades, "grade A raw" and "grade C," have long since been abolished.

The primary function of a health department, as it concerns supervision and control of the milk supply, is the establishment of minimum uniform standards which will assure the community a safe and wholesome product. With this objective in view, it is deemed advisable now to consolidate grade A and grade B pasteurized milk into a single grade. We believe that this aim will be achieved by the standards to be set up for the proposed single grade of milk. There is no more reason today for the department of health to sponsor several grades of milk than there would be to provide in the sanitary code more than one standard of safety for the city water supply or many standards for the wholesomeness of other food products.

Studies of the records of the department of health and of the milk industry indicate that, during 1939, 90 per cent of the grade B milk producers in the milk shed delivered milk to country plants with less than 100,000 bacteria per cubic centimeter, this being the present grade A requirement, and over 90 per cent of the pasteurized milk samples had less than 30,000 per cubic centimeter, the standard for grade A pasteurized milk. The proposed requirements for all milk have been fixed essentially at a point more nearly consistent with the actual quality of grade B milk now supplied to New York City.

To the public the designation "grade B" connotes inferiority. This is entirely undeserved on the basis of the quality or safety of the grade B milk supply sold in this city. Because of this feeling, many families continue to purchase grade A milk when they could more profitably utilize the extra expenditures involved in purchasing larger quantities of milk, which, from a public health standpoint, would be much more desirable.

I feel confident that there is no public health significance in the difference between the present grade A standards and the proposed standards under consideration that will be applicable to all milk. The best proof as to the safety of our grade B milk supply is the fact that there is no record of a single outbreak of disease of milk-borne origin in New York City since pasteurization has been enforced. Furthermore, the diarrheal death rate for children has declined from 9.1 per thousand under 5 years of age in 1911, to 0.8 per thousand under 5 years of age in 1938.

Eighty-seven per cent of the city's milk supply is grade B milk. In providing more stringent legal standards for grade B milk, of which 90 per cent already meets the proposed standards, it is felt that the department of health is taking a progressive step in line with the action of many other large municipalities in this country.

WILLIAM H. BEST, M.D., New York.
Deputy and Acting Commissioner of Health.

MOTTLED ENAMEL

To the Editor:—Drs. G. V. Black and Frederick S. McKay, when they began an investigation of endemic mottled enamel in Colorado about twenty-five years ago (*Dental Cosmos* **58**:129, 1916), started something which has provoked much discussion and genuine interest. The physical plight of mottled teeth is such as to cause both physicians and dentists to seek diligently for effective measures of prevention. The dentists are without means of restoring these teeth to normal. In order to eliminate an uncomely, often repulsive, appearance because of severely fluorosed front teeth, our dentist friends are forced to substitute porcelain crowns or artificial dentures for these malformed members. But, as has been pointed out by Dean and others (*Pub. Health Rep.* **54**:862 [May 26] 1939), the incidence of caries in the mottled teeth is significantly lower than in normal teeth. Why and how does this occur? So far as I know, this is still an unsolved puzzle. Perhaps Atkins (Dental Caries, Chicago, American Dental Association, 1939) has offered a clue that merits some "follow-up" and "tracing down." This investigator was able to effect a reduction of slightly more than 85 per cent in the aciduric cell (yeast, Bacillus acidophilus, oral cocci) count of the mouth in a series of twenty cases (the percentage of reductions is not stated in Atkins's paper but was submitted to me later) by using, as a mouth wash, water bearing 5 parts per million of fluorine.

No restrictions of diet nor habits were imposed. Indeed, each was allowed all the sweets desired, which privilege some of the children enjoyed to the fullest. The only requirements were the careful brushing of the teeth immediately after each meal, followed by thorough rinsing of the mouth with water bearing fluorides in a concentration of 5 parts per million. Specimens of saliva for bacteriologic study were collected rather uniformly at about 4 p. m., never immediately following the prophylaxis of the mouth.

According to Hadley (Quantitive Determination of Lactobacillus, *J. Dent. Research* **13**:415 [Oct.] 1933), Fosdick (Northwestern University Bulletin on Dental Research, Aug. 2, 1939) and others, caries susceptibility varies directly with the aciduric cell count level, i. e. a high count indicates a high degree of susceptibility and a low or negative count always means low susceptibility or complete immunity. If this is true, apparently

Atkins has pointed the way toward reducing the incidence of caries susceptibility by means of minute quantities of fluorine applied topically as a mouth wash without exposure of the patient to the hazards of mottled enamel.

MARVIN F. HAYGOOD, M.D., M.P.H.
State Health Department,
Des Moines, Iowa.

EFFECT OF EXTERNAL TEMPERATURE ON SEDIMENTATION RATE OF RED BLOOD CORPUSCLES

To the Editor:—In a recent issue of THE JOURNAL (Dec. 2, 1939, p. 2079) appeared a communication from Dr. A. S. Wiener with reference to the erythrocyte sedimentation test. He referred to unpublished observations in which he and his co-workers noted the effect of external temperature on the sedimentation rate.

As there is but little in the literature on this phase of the sedimentation rate, I refer to similar observations which were published in 1928 (Gordon, M. B., and Cohn, D. J.: The Effect of External Temperature on the Sedimentation Rate of the Red Blood Corpuscles, *Am. J. M. Sc.* **176**:211 [Aug.] 1928). In our studies we divided each sample of blood into three parts and each portion was placed under a different temperature (10 C., 23 C. and 37 C.) and permitted to sediment at that temperature. In some instances, after the first test, the tubes were interchanged and retested at new temperatures.

We drew the following conclusions: "External temperature exerts an influence on the sedimentation rate of the red blood corpuscles. Higher temperatures accelerate the rate and lower temperatures diminish the velocity. Intermediate temperatures give intermediate results. All observations on the sedimentation test must be performed under properly controlled conditions with a standard known temperature. Seasonal variations showing the effect of extreme heat in the summer and of cold in the winter must be taken into consideration in the interpretation of results unless controlled by uniform standard experimental conditions."

MURRAY B. GORDON, M.D., Brooklyn.

CITRATE METHOD OF BLOOD TRANSFUSION

To the Editor:—In a recent letter from Buenos Aires (THE JOURNAL, March 2, p. 816) your correspondent stated that Agote, in November 1914, was the first to use sodium citrate in the transfusion of human blood. This statement requires correction. Seven months before Agote, Hustin (Note sur une nouvelle méthode de transfusion, *Soc. roy. d. sc. méd. de Bruxelles* **72**:104 [April 6] 1914) used citrated blood, though in a strongly diluted form. As Hédon (Note complémentaire sur la transfusion du sang citraté, *Presse méd.* **30**:57 [Jan. 31] 1918) pointed out, Hustin's method was really an infusion of strongly diluted blood mixed with sodium citrate and dextrose.

It was a curious coincidence that both Agote's (Nuevo procedimento para la transfusión del sangre, *An. Inst. modelo de clin. méd.*, January 1915), and my (A New and Greatly Simplified Method of Blood Transfusion, *M. Rec.* **87**:141 [Jan. 23] 1915) first publications of the new method of citrate transfusion occurred in the same month (January 1915) just twenty-five years ago.

Agote's article did not report any experimental work on the interesting problems involved in this question. He simply stated that he gave small transfusions of citrated blood (300 cc.) to two patients. His work left unanswered the question whether transfusions of average size (from 500 to 700 cc.) could be given with this method without causing toxic effects. Furthermore, he did not study the effect of anticoagulants on the coagulation time of the recipients. These questions were answered in my paper (January 1915) in which I reported in detail about my experimental work, which had extended over six months. At the same time I reported two human transfusions of 300 and 500 cc. respectively.

I think that in fairness to all concerned it must be stated that citrated blood transfusion was originated contemporaneously and independently by Agote and myself.

I have always felt that the rapid popularization of the method and its extensive use in the World War was due to the fact that the careful experimental work which I reported in my first paper on this subject had put the method on a safe basis.

RICHARD LEWISOHN, M.D., New York.

STANDARDIZATION OF BLOOD PRESSURE READINGS

To the Editor:—The report by the Committee for the Standardization of Blood Pressure Readings of the American Heart Association (THE JOURNAL, July 22, 1939, p. 294) contains the following statement: "If the radial pulse is felt at a higher level than that at which the auscultatory sound is heard, the palpatory reading should be accepted as the systolic pressure; otherwise the auscultatory reading should be accepted."

The natural inference from this must be that if the auscultatory reading is higher than the palpatory, the former is correct. I wish to call attention to one important exception to this general rule: There are instances in which the heart beat is so violent that sounds are transmitted from the top of the cuff downward, so that they are audible below the cuff for 50, 100, 200 or more millimeters higher than the level at which the pulse comes through at the wrist. This is true in an occasional case of free aortic insufficiency with marked hyperactivity of the peripheral vessels. I have seen an instance in which a physician thought that the blood pressure was 200 or more in a girl aged 15 years. On careful examination I found that the pulse first appeared at the wrist when the blood pressure reading was 145, although clearcut sounds could be heard below the cuff at levels of 200, 250 and even 300 mm.; in fact, it would not have mattered how great had been the constriction in that blood pressure cuff, for the sounds were merely transmitted from above to below the cuff. In such cases the palpatory method is the only satisfactory one to detect the pressure level.

S. A. LEVINE, M.D., Boston.

GERIATRICS

To the Editor:—A recent communication was published in THE JOURNAL referring to the word geriatrics. I frequently read articles on this subject advising its study and suggesting that young men take it up as a specialty. So far as I know, no one has as yet announced himself as a geriatrist, and for a very good reason.

The analogy to pediatrics is basically unsound. The child has no objection to being a child and knows that he will soon get over it, while the oldster has been dreading old age all his life and knows that it will not only continue but get worse. He does not want to admit to himself or to any one else that he is growing old, and he would certainly be reluctant to go to a doctor who is specializing in old age and its ailments.

There are very few disorders that are strictly limited to old age, and the principal one, prostatism, is already in the field of genito-urinary surgery. The other degenerative diseases are properly problems for the internist. The field of internal medicine is already being split up into cardiology, gastro-enterology and hematology, and now the proposal is to segregate the aged. It seems as though rather than talking about preserving the status of the general practitioner there should be a movement started to keep the field of internal medicine intact.

PAUL W. KNISKERN, M.D., Grand Rapids, Mich.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

FOOTBATH SOLUTIONS FOR RINGWORM

To the Editor:—I would appreciate authoritative answers to the following questions with regard to solutions to be used in foot pans or foot wells by bathers in going to and from the shower rooms and for the prevention of "athletic foot," or phytosis of the foot. 1. Which is to be preferred for its efficacy, calcium or sodium hypochlorite? 2. What strengths of each should be used to represent equivalent solutions? 3. What is the approximate amount of free or available chlorine that will be given by each? 4. What is the approximate or relative costs of the two per unit of available chlorine?

Richard K. Kimmel, M.D., St. Louis.

ANSWER.—1. Sodium hypochlorite.

2. One per cent sodium hypochlorite and 2 per cent calcium hypochlorite.

3. Approximately 0.9 to 1 per cent of available chlorine corresponding to 1 per cent sodium hypochlorite or 2 per cent calcium hypochlorite.

4. Calcium hypochlorite is generally cheaper than sodium hypochlorite, depending on the source of supply, containers, transportation, and other factors. There have been no studies on the fungicidal or fungistatic capacity of calcium hypochlorite. It is more irritating to tissues than sodium hypochlorite and has the additional disadvantage of producing a deposit of lime (calcium hydroxide) as the free chlorine is given off. Sodium hypochlorite is conveniently purchased in metal chemical carboys in 20 per cent strength. This is diluted twenty to one for placing in footbaths and the solution should be changed every second or third day. The approximate cost per change should be about 10 to 15 cents, depending on the size of the footbath.

CYANOSIS AND HYPERPYREXIA IN NEWBORN

To the Editor:—Recently I was called to see a baby at 2 p. m. which had been born without medical attention thirty-six hours before. To all appearances the infant was dead. I removed its clothing and during this handling it made a feeble effort to breathe. No action of the heart could be detected. The child was severely cyanotic. The body felt quite warm, so I placed a thermometer in the rectum, which registered 109 F. The procedure was repeated with the same result. I placed the infant in a tepid bath (water 102 F.) and injected four drops of epinephrine into the heart. In two minutes the radial pulse could be felt and the child was breathing. However, it remained in a listless condition and made no effort to cry but opened its eyes many times. The night before it had been restless and had cried almost all the time, I was informed. When I left, an hour later, the infant had a temperature of 101 F. and was quiet. I informed the parents that the child would not live, because such temperatures as it had sustained were bound to produce irreparable damage of some kind. It died at 6 p. m. This is the first case of its kind I have observed. What could have happened? It could not have had any disease, and no disease would produce a temperature of 109 F. Could an injury to the brain during birth have caused chemical disintegration of such rapid process as to cause such a result?

T. H. Standlee, M.D., Miranda City, Texas.

ANSWER.—The data presented in this query are hardly adequate to present the basis for a definite opinion regarding the underlying conditions that would cause a 36 hour old newborn infant, cyanotic and stuporous, to have a temperature of 109 F. by rectum. The heat regulating mechanism in newborn infants is labile. A premature infant is an example of this malfunction of the heat regulatory mechanism. It has been noted in a large premature ward on hot summer days when the outside temperature readings of 95 to 100 were recorded that the premature babies in the ward all showed some degree of hyperthermia, rectal temperatures of 100 to 102 having been observed. Newborn infants who are too warmly swaddled may show a rise in temperature. A newborn infant smeared with goose grease and wrapped in woolen blankets showed a rectal temperature of 106 F. on a hot summer night. When a newborn infant is not offered sufficient foods by mouth a so-called dehydration fever may occur which is quickly relieved by giving adequate oral food. However, this condition would hardly account for the cyanosis noticed in the infant mentioned in the query. Among the pathologic conditions which may show hyperthermia to a considerable degree are miliary tuberculosis, malaria, brain injury, peritonitis, Still's disease and sepsis. The most probable cause in this case was a breakdown of the heat regulatory center in the medulla, possibly due to hemorrhage sustained at birth.

BLOOD COUNT IN SHOCK AND HEMORRHAGE

To the Editor:—Of what value is the blood count (particularly with reference to the white cell count and the differential) in determining the presence of internal (intra-abdominal) hemorrhage in recent abdominal injury in which there is shock and obscure abdominal signs? What may the blood count (white blood count and differential) be in traumatic shock alone?

Stanton S. Eddy Jr., M.D., Middlebury, Vt.

ANSWER.—This is a valuable and practical question but is difficult to answer in full authoritatively. It would seem to be an inviting subject for study in a large series of cases. It is probably impossible to distinguish between shock and hemorrhage by means of the blood picture alone, as leukocytosis may occur in both conditions. T. G. Orr (in Lewis's Practice of Surgery, volume 1, chapter 9, page 16) says: "Following severe trauma a leukocytosis as high as 20,000 or even higher may develop within one or two hours." The count rapidly diminishes. In shock there is a concentration of blood in the capillaries. R. L. Haden (personal communication) says: "I do not believe . . . there is very much leukocytosis after shock which is not associated with hemorrhage. There is, of course, hemoconcentration with shock, and this is the explanation for the rise in the red cell count. With this there would necessarily be a slight increase in the leukocyte count, but this is only relative and not absolute."

After hemorrhage, leukocytosis develops rapidly. Castle and Minot (Pathologic Physiology and Clinical Description of the Anemias, London, Oxford University Press, 1936, p. 26) say: "Within ten minutes after a considerable hemorrhage the blood platelets in circulation will be found increased and the coagulation time of the blood shortened. Almost as rapid is the leukocytosis due to an outpouring of young granular leukocytes. This effect reaches its maximum in two to five hours. . . . With rapidly repeated hemorrhages producing extremely severe anemia, the white cells may reach 35,000 per cubic millimeter."

Whitby and Britton (Disorders of the Blood, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1937, p. 82) say: "A great loss of blood is followed by a moderate neutrophil leukocytosis, which appears within a few hours." The eosinophil count diminishes. These authors say that "if the hemorrhage occurs into one of the serous cavities, or into the meninges, or into a joint, a leukocytosis of from 18,000 to 30,000 cells per cubic millimeter is to be expected." The leukocyte count is maximal in about ten hours and lasts three or four days. In progressive hemorrhage there is, of course, a decrease in the concentration of red blood cells and hemoglobin.

The following references also should be consulted:

Bilalock, Alfred: Trauma; Occupational Diseases and Hazards; Shock and Hemorrhage, *Bull. New York Acad. Med.* **12**:610 (Nov.) 1936.
Boyers, L. M.: Shock: A Study of the Partial Available Modern Literature of Shock, *Am. J. Surg.* **36**:623 (June) 1937.
Harkins, H. N., and Roome, N. W.: Concealed Hemorrhage into Tissues and Its Relation to Traumatic Shock, *Arch. Surg.* **35**:130 (July) 1937.

PAINFUL PARESTHESIAS AFTER TRIGEMINAL ROOT RESECTION

To the Editor:—A woman aged 68 had a complete resection of the trigeminal nerve root performed six months ago for neuralgia of the first and second branches of the fifth nerve. Since the operation she has been experiencing continuous severe discomfort over the entire portion of the face and eye rendered anesthetic. These sensations are described as burning, tearing, pulling, sticking, coldness and the like and are in no way similar to the pain experienced prior to operation. The patient has never before displayed any neurotic tendencies. Sedation, analgesics, heat and suggestion have proved of no avail, and time has shown no tendency to effect a cure. The patient is my mother and I am at a complete loss as to what else I can do to relieve this terrible discomfort she is unquestionably suffering.

M.D., New York.

ANSWER.—So-called painful paresthesia in the anesthetic area following resection of the trigeminal sensory root for major trigeminal neuralgia is not, unfortunately, a rare condition. A search through the literature for the cause and an adequate treatment of this disturbing postoperative condition, as well as experience in a large series of cases, does not reveal an adequate answer to the question here asked. This condition is most likely to occur in patients of or past middle age, and it makes its appearance a few weeks after the operation when the initial effects of sudden relief from pain and sudden facial anesthesia are past. It is most often seen in patients who lead a leisurely life with no definite occupation and who have time to take notice of their complaint. It is seldom complained of by a busy housewife, a hard working laborer or any person engaged in enjoyable, time consuming pursuits. Though the case in question would not seem to be on a psychoneurotic basis, it is frequently true that psychotherapy helps such patients. One must make certain too that the original disturbance was a true major trigeminal neuralgia and not an atypical neuralgia or peculiar type of head

pain. This painful complex has occurred in cases in which a partial root resection has been performed with preservation of the ophthalmic division and a second operation, with resection of the remaining fibers, has not stopped the severe discomfort. It has been assumed that the disturbance is due to a lesion in the nucleus of the fifth nerve, nutritive in nature and based on localized arteriosclerotic changes or hypertension. Some hold the optic thalamus responsible for the painful sensations. Theoretically, section of the fibers between the fifth nucleus and the thalamus would stop the pain, but this is impossible at present for all practical purposes. Cervical sympathectomy has been done in some cases with temporary relief or permanent partial amelioration of the pain. Drugs, rest, change of occupation and ordinary suggestion do not help in the majority of cases. The condition is conceded to be intractable; the cause is unknown and a satisfactory treatment is lacking. The following references are suggested as a source of information on this subject:

Lewy, F. H., and Grant, F. C.: Physiopathologie and Patho-Anatomic Aspects of Major Trigeminal Neuralgia, *Arch. Neurol. & Psychiat.* **40**: 1126 (Dec.) 1938.
Olivecrona, Herbert: *Acta chir. Scandinav.* **82**: 99.

CRYSTALLIZED VIRUS—BOOKS ON VIRUSES

To the Editor:—1. I have been told that Stanley, of the Rockefeller Institute, has extracted the virus of tobacco leaf mosaic disease and finally reduced it to a pure state and that this final pure state is a crystal. It is as dead as a crystal of table salt or, for that matter, a brickbat. If a crystal of this is placed on a healthy leaf, the leaf becomes infected and the disease then spreads through the whole field of tobacco which was formerly free from it. Having reproduced itself thus greatly, it can be extracted from the newly diseased leaves in quantity and again reduced to the pure crystalline state, which is as dead as ever. Is this description essentially correct? If so, is it not a truly colossal discovery in biology and especially important to medicine? Why has it not received the Nobel prize? 2. Please give me the names of three or four books giving the latest and most up-to-date information on viruses: not books which are too technical and difficult and written for specialists, but books such as would be satisfactory for the average physician.

J. A. McKay, M.D., Mercer, Pa.

ANSWER.—1. Dr. W. M. Stanley crystallized the virus of tobacco mosaic in 1935. The crystals are considered to be chemically pure. When the crystalline material is in solution it is capable of producing a disease in tobacco plants which is transmissible in series from plant to plant. This is a discovery of great biologic significance. As yet, however, no consensus has been reached concerning the nature of the crystalline material. It has many of the properties of living agents and some of the characteristics of large molecules. Certain workers, in spite of the crystalline nature of the virus, believe that it is alive, while others consider it an inanimate material reproduced by processes of autocatalysis.

2. Two books regarding viruses and virus diseases suitable for the medical profession in that they are not too technical are "The Lane Medical Lectures: Viruses and Virus Diseases," by Thomas M. Rivers, M.D., published by the Stanford University Press, Stanford University, Calif., 1939, price $1.75, and "Virus and Rickettsial Diseases with Especial Consideration of Their Public Health Significance," by a group of scientists in the Harvard Medical School, published by the Harvard University Press, Cambridge, Mass., 1940, price $6.50.

"SEKOV" OBESITY CURE

To the Editor:—A pamphlet describes a weight reducing cure called "Sekov." I know several patients who have lost from 30 to around 100 pounds within one to two years. Is there anything in this medication which would be dangerous or could it be taken under medical supervision, controlled by blood pressure, basal metabolism and the like?

M.D., California.

ANSWER.—The weight reducing "cure" referred to was tested by the Los Angeles Health Department in August 1936 for dinitrophenol, but the sample tested was not found to contain any of this substance, and the report of that department quoted two formulas which it said were supplied by a saleswoman for this item ("Sekov") and which are as follows:

No. 1.—Thyroid 1½ gr.
Big pill whole Pit. 1 gr.
" Ovar. 3 gr.
R ½ is ½ of No. 1. Digitalis ½ gr.

No. 2.—Rhubarb root 2 gr. Cascara Sagrada 1 gr.
Aloin ⅛ gr. Asafetida ½ gr. Oleoresin-ginger ⅛ gr.
T. ½ size. Digitalis ½ gr. Thyroid 2 gr.
P. ½ size. Whole Pit. 2 gr. Thyroid 1 gr.
O. ½ size. 2 gr. Ova. whole. 1 gr. whole Pit.

If these formulas were true statements of composition and the composition of the item has not been revised since that time, it is perfectly obvious that the effects of taking these pills will naturally result in the reduction of weight in many cases. It goes without saying that self medication with such substances as thyroid, pituitary, ovarian extracts and digitalis is contrary to the best interests of the patient. If it is advisable for the patient to reduce, he should use only such drugs as are prescribed by the physician on the basis of his examination and as modified according to the effects produced. This item is just one more example of the fact that "obesity cures" are either composed of ineffectual ingredients or else they contain drugs which, although they produce the desired effect, should not be used in self medication.

The following information was released by the Federal Trade Commission on Feb. 19, 1940:

"The U. S. District Court for the Southern District of California has issued a preliminary injunction upon petition of the Federal Trade Commission, forbidding Sekov Corporation, and Edwin W. Vokes and Hazel Ruth Vokes, officers of the corporation, and as individuals trading as Sekov Reducing Studios, all of 6404 Hollywood Blvd., Hollywood, Calif., from further dissemination of false advertising pending issuance of a complaint by the Commission under its regular procedure and until final disposition thereof.

"It was alleged that the preparations advertised and sold as 'Sekov Reducer' and as 'Sekov,' and represented to be safe, competent and scientific treatments for obesity, contain drugs which, if used as prescribed in advertisements of the defendants or under conditions that are customary or usual, might result in serious or irreparable injury to the health of users."

IODIZED POPPY-SEED OIL FOR ASTHMA

To the Editor:—Can you give me any information regarding the treatment of bronchial asthma by intratracheal injection of iodized oil as reported in the *New York State Journal of Medicine* **36**: 1151 (Aug. 15, 1936) by Dr. William Anderson?

J. M. Greenhouse, M.D., St. Louis.

ANSWER.—The early reports on the use of iodized oil for the treatment of bronchial asthma were for the most part favorable:

Pritchard, Stuart; Whyte, Bruce, and Jordan, J. K. M.: Use of Iodized Oil in Diagnosis and Treatment of Bronchial Affections, THE JOURNAL, April 10, 1926, p. 1119.
Ochsner, Alton: Bronchography Following the Passive Introductions of Contrast Media into the Tracheobronchial Tree, *Wisconsin M. J.* **25**: 544 (Nov.) 1926.
Ochsner, Alton: An Unappreciated Cause of Chronic Bronchitis, THE JOURNAL, July 20, 1929, p. 188.
Taylor, J. H.: Treatment of Asthmatic Bronchitis with Iodized Oil, *Minnesota Med.* **15**: 408 (June) 1932.
Fink, L. W.: Lipiodol as Therapeutic Agent, *ibid.* **15**: 522 (Aug.) 1932.
Cole, D. B., and Harper, Edgar C.: Therapeutic Use of Iodized Oil in Pulmonary Disease, *J. Lab. & Clin. Med.* **18**: 704 (April) 1933.
Alison, J. F.: Treatment of Asthmatic Bronchitis with Iodized Oil, *South. M. J.* **26**: 696 (Aug.) 1933.
Amberson, J. B., Jr., and Riggins, H. M.: Lipiodol in Bronchography: Its Disadvantages and Dangers and Uses, *Am. J. Roentgenol.* **30**: 727 (Dec.) 1933.

Its good results have been ascribed both to a presumed bactericidal effect and to mechanical upward displacement of bronchiolar plugs by the iodized oil. William Anderson (Some Observations on the Value of Intratracheal Injections of Iodized Oil for Bronchial Asthma, *J. Allergy* **6**:44 [Nov.] 1932; The Treatment of Bronchial Asthma by Intratracheal Injections of Iodized Oil, *New York State J. Med.* **36**:1151 [Aug. 15] 1936) and Balyeat (Balyeat, R. N., and Seyler, L. E.: The Therapeutic Value of the Intratracheal Use of Iodized Oil in Bronchial Asthma, *Journal-Lancet* **54**:563 [Sept. 15] 1934. Balyeat, R. M.; Seyler, L. E., and Shoemaker, H. A.: The Diagnostic and Therapeutic Value of the Intratracheal Use of Iodized Oil in Cases of Intractable Asthma, *Radiology* **24**:303 [March] 1935) have been especially enthusiastic and report large numbers of cases with excellent results.

In other hands, however, less favorable results have occurred. In an article which summarizes forty cases of intractable asthma, L. H. Criep and J. W. Hampsey (*J. Allergy* **9**:23 [Nov.] 1937) state that improvement occurred in only four; the remaining thirty-six were failures. In addition, these authors collected 267 other cases treated by sixty-four men prominent in the fields of allergy and otolaryngology. Cures were obtained in only 1.9 per cent of these and improvement in 24.7 per cent; there were 73.4 per cent of failures. Two thirds of these specialists have discontinued the use of iodized oil because of poor results.

Most specialists in this field are now agreed that iodized oil should be tried only in those cases in which asthma continues after skilful allergic management has been given a thorough trial, this to include a careful history and physical examination, complete cutaneous tests and treatment along allergic lines for not less than from six to twelve months.

There are two commonly used methods of instilling iodized oil. It can be given directly by tracheal cannula, nasal tube or bronchoscope or by dropping the oil on the back of the tongue while the tongue is pulled forward and the patient breathes

rapidly; the latter method can be easily carried out in most cases without local anesthesia.

Iodized oil remains in the bronchioles for varying periods and should not be used for patients who are sensitive to either iodine or poppy-seed, the oil of which is usually the vehicle for the iodine. Recently Balyeat himself (*Balyeat Hay Fever and Asthma Clinic Quarterly* 9:2 [Nov.] 1939) seems to have become less enthusiastic.

DIAGNOSIS OF HEADACHES

To the Editor:—A white man aged 30 has been subject to severe migrainous attacks on the left side for the past twelve years. He never vomits but feels nauseated, has a tendency to sneeze and experiences a "stuffiness" in the left nostril. The left temple is tender but the carotid areas are not. Alcohol will quickly precipitate an attack. There is a family history of migraine but no personal allergy. The headaches are not relieved by ergotamine tartrate or epinephrine (never given intravenously). Treatment with histamine as recently outlined by Horton for "vascular headaches" has been apparently of no avail. The patient resorts to considerable morphine in order to obtain relief. I do not believe he is addicted. He was recently studied in a nearby clinic and desensitization to a number of allergens was suggested and tried with little or no result. Extensive laboratory tests including Kahn, Wassermann, sinoil roentgenogram and blood chemistry were negative. A devitalized left second molar was found. His basal metabolic rate was minus 16. Thyroid therapy did not seem to help. Physical examinations, including neurologic, have always been essentially negative. His blood pressure is 100 systolic, 60 diastolic. Within the past month he has had many attacks of severe substernal pain without severe dyspnea. At times his headache will cease abruptly and the chest pain start and vice versa. This has strengthened a previous opinion that the chest pain is "migraine." Roentgenograms of the chest are negative. The heart seems normal. What suggestions can you offer as to diagnosis and further management?

J. Paul Proudfit, M.D., Washington, Pa.

ANSWER.—With headache on the left side occurring in a person who has a family history of migraine but whose headaches are not relieved by ergotamine tartrate, a diagnosis of migraine cannot be confirmed without further information. On the other hand, if compression of the left temporal artery significantly alters the headache during an attack, ligation and section of this artery are indicated. It would be advantageous to know the effect of 1 cc. of ergotamine tartrate given subcutaneously at the onset of an attack or the result of half this amount by vein. The substernal pain complained of is a rare occurrence, which one would hesitate to call "migraine."

The patient may have a nonspecific inflammation of the left frontal sinus with resultant left-sided neuralgia. Under these circumstances, removal of the left turbinate might be successful and treatment by inhalation of 1 per cent ephedrine in physiologic solution of sodium chloride is also to be recommended. The use of capsules containing ¾ grain (0.024 Gm.) of propadrine and 1/250 grain (0.00022 Gm.) of atropine sulfate is sometimes also effective.

The hypotensive factor might be attacked by the use of from 5 to 20 mg. of benzedrine sulfate daily.

If therapy directed toward nasal congestion and sinus occlusion is ineffective, as it may well be in this case, attention should be centered on means of proving involvement of the left temporal artery as the cause of the pain (Graham, J. R., and Wolff, H. G.: Mechanism of Migraine Headache and Action of Ergotamine Tartrate, *Arch. Neurol. & Psychiat.* 39:737 [April] 1938).

A paper entitled "Precordial Migraine" by Thomas Fitz-Hugh Jr. appeared recently in *International Clinics* (1:141 [March] 1940).

EFFECT OF FREEZING AND COOKING ON VIRULENCE OF PASTEURELLA TULARENSIS

To the Editor:—I am frequently asked about tularemia and should like an answer to the following questions: 1. Does freezing of the rabbit as is done in the commercial lockers minimize the danger of tularemia? 2. Is cooking or frying the meat until the color changes to gray sufficient to eliminate all danger of tularemia?

M.D., Kansas.

ANSWER.—1. At the third International Congress for Microbiology, held in New York Sept. 2 to 9, 1939, Dr. Edward Francis of the National Institute of Health, U. S. Public Health Service, Washington, D. C., made the following statement with regard to the freezing of rabbit carcasses infected with tularemia:

"Artificially infected rabbit carcasses, unmutilated except for removal of stomach and intestines at the moment of death, were immediately frozen at —14 C. and thereafter kept continuously at that temperature without thawing. At six month intervals, tissues of the rabbits were tested for survival of infection by injection into guinea pigs. Virulent organisms of Bacterium tularense [Pasteurella tularensis] survived forty-two months in spinal cord, thirty-six months in brain, eighteen months in spleen, twelve months in muscle and liver, and five months in bone marrow. Heart blood of guinea pigs, drawn in half cubic centimeter amounts, into glass pipets which were then sealed at each end and kept continuously at —14 C., was found virulent when tested at six month periods up to twenty-four months but not longer.

"A culture of Bacterium tularense was frozen in a block of carbon dioxide snow at —56 C. and was fully virulent when thawed, i. e. it survived a temperature of about 70 below zero Fahrenheit."

2. Thorough cooking will destroy the organism in infected tissues. Exposure to from 56 to 58 C. for ten minutes will kill Pasteurella tularensis in cultures and in splenic tissues. The cooking of infected rabbit meat which permits red muscle or red juice to remain near the bone does not kill virulent Pasteurella tularensis.

HEMOGLOBIN COLOR SCALES

To the Editor:—I have before me a Feosol hemoglobin scale (improved Tallqvist) and an improved hemoglobin scale put out by Amsco Products, and there is a tremendous difference in the shades, particularly in the range from 20 per cent to 60 per cent. Can you tell me which is correct and, if neither, what scale one can get that is approximately correct?

Carl R. Doten, M.D., Providence, R. I.

ANSWER.—Most hemoglobin color scales of the Tallqvist type, including the Amsco scale, have much lighter shades of color than the Feosol hemoglobin scale in the range between 20 and 60 per cent. A check with blood samples of known hemoglobin concentration in the lower ranges reveals that the Feosol scale is approximately correct, whereas the readings on the Amsco scale are too high. The most that can be expected of any Tallqvist scale is an approximation of the true hemoglobin value. The Sahli-Hellige hemometer and the Haden-Hausser hemoglobinometer are relatively inexpensive and give accurate results.

"GATCH" OF HOSPITAL BED

To the Editor:—We have been having some discussion as to just what the term "Gatch" means when used in connection with hospital beds. Does it refer to the frame which makes possible the change of position, to the spring itself or to both?

J. Howard Beard, M.D., Urbana, Ill.

ANSWER.—The term "Gatch" used in connection with hospital beds refers to the bed bottom or frame that is supported by head and foot pieces. It includes the frame and the mechanically operated spring parts. This type of frame and spring or bed bottom has also been designated by some manufacturers as the "Mount Sinai" bed bottom. Various other designations are also used in other equipment catalogues.

CONTINUED USE OF SACCHARIN

To the Editor:—A person with a tendency to overweight desires to reduce the number of calories ingested. Need any harm be anticipated if he habitually uses saccharin instead of sugar in sweetening his tea and coffee? The amount of saccharin used is about 1½ grains (0.1 Gm.) daily.

M.D., Connecticut.

ANSWER.—Investigations of saccharin have failed to show any harmful effect except in extremely large doses. There seems to be no reason why saccharin may not be continued in average sweetening doses for an indefinite period. In fact this has been done by many diabetic patients without any noticeable effects.

STERILIZATION OF OBSTETRIC INSTRUMENTS BY AUTOCLAVING

To the Editor:—Does it remove the temper to sterilize obstetric forceps and craniotomy instruments in an autoclave? How long would the instruments be sterile if wrapped in several layers of muslin?

Richard Turpin, M.D., Augusta, Ga.

ANSWER.—The reasons for not autoclaving delicate sharp-cutting instruments such as scalpels, cataract knives or even scissors would seem not to apply to the sterilization of obstetric forceps and craniotomy instruments. Any loss of temper due to repeated autoclaving would probably not interfere with the purposes for which these instruments are used.

If wrapped in a sufficient number of layers of muslin and then autoclaved and the steam evacuated at the end of autoclaving so that the package is dry, these instruments should remain sterile indefinitely.

LOCAL REACTION TO VACCINE

To the Editor:—In The Journal, January 13, page 182, the reply to the query as to the causes of local reactions from a toxin vaccine does not mention the usual reason in the case of vaccines prepared as described. This is the acid reaction developed in the vaccine medium, which should be corrected by titration with a sterile sodium hydroxide solution. The reaction due to hypersensitiveness to bacteria or medium proteins can be reduced or eliminated by rebuilding the vaccine to subdivide the protein molecule.

K. P. A. Taylor, M.D., Panama.

Council on Medical Education and Hospitals

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

Thirty-Sixth Annual Meeting, held in Chicago, Feb. 12 and 13, 1940

(Concluded from page 1485)

DR. ROY B. HARRISON, New Orleans, in the Chair

THE FEDERATION OF STATE MEDICAL BOARDS

FEBRUARY 13—MORNING

The Refugee Physician

DR. JOSEPH PRATT, Boston, and DR. IRVING GRAEF, New York: The recent immigration of foreign physicians has created problems which require candid discussion and a thorough exploration, since they affect our community and the immigrants who are to become new citizens in it. The National Committee for Resettlement of Foreign Physicians, which I represent with its affiliated committees in different states began its functions on Feb. 1, 1939, and has tried to work out a constructive and mutually beneficial program to solve the problems presented by the refugees. Our central office has registered 1,646 foreign physicians who immigrated to the United States between 1933 and Jan. 1, 1940. We know that between 800 and 900 additional refugees had become more or less established in institutional work or in practice prior to our registration. Numerically the refugee physicians do not constitute a group of indeterminate size, and since wartime conditions and other countries are absorbing the remainder, the reservoir for continued immigration is empty, or nearly empty.

Our committee contends that as long as those who have come are bona fide legal immigrants who have taken out their first papers, they are entitled to fair consideration as future citizens, in accordance with the traditional United States policy. The problems created in the ports of entry, such as New York, are becoming acute. Primarily the tension has increased because there are only four states left where only naturalization papers are required before taking the licensing examinations. These are Massachusetts, Connecticut, New York and Maryland, and they are the states that are least in need of more physicians. Illinois has admitted to examination those who have had one year's internship or its equivalent in an American hospital in addition to first papers. Ohio admits older men, if naturalized, to examination but requires thirty hours of collegiate training in America of men graduated after 1920. In New York City there are between 1,300 and 1,600 foreign physicians, of whom from 950 to 1,000 are still unlicensed and are preparing for examinations. Our primary aim is to promote settlement only in districts actually short of physicians. There is evidence that whole counties in some states are without a single resident physician. Here is an opportunity to promote the medical welfare of those in need of it and at the same time to enrich rural life with the cultural resources of many of the émigré physicians.

In less than one year this committee and affiliated groups have resettled about 400 refugees, and we have been most favorably impressed with their assimilability and their warm acceptance by the committees or institutions in which they have settled.

A branch of this committee in New York City has set up twenty examining boards in as many specialties. They have interviewed 300 of the registrants in consideration for placement when and if opportunities arise. These boards are composed of nonsectarian groups of prominent physicians and specialists who have certified the qualifications, or the lack of qualifications, after suitable interviews, sometimes supplemented by clinical examination, with the émigré candidate.

The sectarian proportions among our registrants are approximately 25 per cent Christians (of these two thirds are Catholic and one third Protestant) and 75 per cent Jews. About 120 men have been settled in rural New York and we have yet to hear a complaint. Men have been settled in rural Ohio and in rural parts of Illinois, New Jersey, Massachusetts, Maryland, Connecticut and a few in other states. It is gratifying to learn of their cordial reception. Interns have been placed in hospitals in Virginia and North Carolina and other less populous states and we have evidence of their successful adjustment.

The chief problem in the resettlement of émigré physicians is the demand in twenty-eight states that they become citizens before admission to licensing examinations. A five year penalty of economic destitution and probable professional deterioration is thus imposed on most of these people. The requirement of full citizenship causes great hardship to the well trained foreign physician. It compels continued concentration in a few cities and aggravates the situation of the local profession. Where the intention to become a citizen is a requisite qualification for licensure—and we believe it should be—it seems unnecessary to bar or delay these persons from fulfilling their functions if they can pass qualifying examinations. The double requirement of internship in a class A American hospital together with graduation from an American medical school in some states is precluding the licensure of worthy émigrés in those states even though there are vacancies and opportunities for internship or rural practice in the same states. According to a study made recently by the Association of American Medical Colleges there are a great number of approved internships in the United States unfilled because of an insufficient number of native graduates. I believe that if these internships are made available, refugee physicians should be required to take a one year's appointment before appearing before a state licensing board. Hospital intern staffs would become more complete and the émigré would learn American methods. If he did good work he would then have the recommendation of the staff. If he did poorly, the National Committee for the Resettlement of Foreign Physicians would be willing to deal with his case and promote retraining in some other occupation.

Inter-American Relations in Medical Education and Licensure

DR. WALTER L. BIERRING, Des Moines, Iowa: About 600 educators representing all sections of the United States met in Washington Nov. 9 and 10, 1939, under the auspices of the Division of Cultural Relations of the Department of State to explore the possibilities of increasing the interchange of educational interests among the American republics. I will present an outline of the discussions with regard to medical licensure.

In the twenty-one Latin-American republics to the south of us there are forty-nine medical schools: Mexico has eleven, Cuba, Haiti and the Dominican Republic have one each, Nicaragua has two, Guatemala, Honduras and El Salvador have one each, Brazil has nine, Argentina four, Chile three, Colombia three, Ecuador three, Bolivia two and Venezuela two, and Dutch Guiana, Paraguay, Peru and Uruguay have one medical school each. There are no medical schools in Costa Rica or Panama.

The admission requirement to a medical school is almost universally the completion of the secondary school course, with either a maturity certificate or a bachelor's degree in science or letters. The medical course varies. The eight Mexican schools require five years with an additional practical year, Cuba seven years. Of the four Central American schools, six years is required in Nicaragua and El Salvador, while in Guatemala and Honduras the course is seven years. The seven schools in Brazil require six years for the degree of doctor of medicine. The four schools in Argentina are divided, two having six year courses and two requiring a seven year course. Several of the medical schools are more than a hundred years old, and practically all are patterned after the older medical institutions of Europe. Instruction is chiefly by lecture and demonstration. By reason of large student bodies in Latin American universities, bedside teaching is precluded to a large extent. There is consequently greater emphasis on didactic teaching, the amphitheater clinic and outpatient teaching. Competent observers state that this is exceptionally fine in the various university departments. Foreign medical graduates, including those from the United States, are required in all the Latin-American republics to have their diplomas revalidated through official channels and further required to pass a complete examination, written and practical, successfully in the language of the country before being granted a license to prac-

tice. In a letter Dr. Hugh S. Cumming, director of the Pan-American Sanitary Bureau, Washington, D. C., said "There is evidence of a general desire in all Latin-American countries to tighten laws governing the practice of medicine in order to restrict as much as possible entrance of foreign graduates, especially from Europe. In fact, there is quite a demand for the abrogation of reciprocity treaties, even with neighboring countries. On the other hand, the authorities, led by humanitarian reasons, have recently in a number of cases let the bars down to physicians from Europe. In Mexico over 100 Spanish physicians have been allowed to enter in the last two or three years. Complaints have arisen in this case since these physicians were supposed to devote themselves exclusively to the care of their countrymen affiliated with a Spanish welfare association and a number of them have apparently engaged in private practice."

In comparing the standards of medical education and licensure in this country with those existing in the Latin-American republics, one can foresee a similar difficulty in establishing treaties or agreements of reciprocity in medical licensure between the United States and the republics south of the Rio Grande. The consensus expressed at the Washington conference was the need of a better mutual understanding of methods of procedure and knowledge of the opportunities available for medical education on the part of the United States and the twenty-one Latin-American republics. The greatest difficulty is the lack of a thorough knowledge of another language.

There are many opportunities in medical education available for interchange of students, fellowships and lectureships. The conference presented the following recommendations:

1. That a study and analysis of medical education, medical schools and research institutes in the Latin-American republics be undertaken, largely for the purpose of comparison with existing educational conditions in the United States.

2. That reciprocal exchanges of biblio film between medical libraries in the American republics be undertaken, and that similar loan collections be exchanged between the Army Medical Museum and museums in the other American republics.

3. That information on medicine, nursing, public health, dentistry and sanitary engineering be collected and exchanged through summaries of literature of the American republics.

4. That public health education of general teachers in the other American republics be encouraged.

Some Social Implications of the Licensure Program

FRANCES P. DE LANCY, PH.D., Morgantown, W. VA.: The immediate aim of professional licensure is to guarantee a minimum standard of ability and practice. Indirectly, however, licensure tends to limit the number of practitioners, to regulate competition and to invest the profession with a greater or lesser degree of social prestige. This scheme of professional licensure has produced certain commendable results. It has placed the solution of scientific problems in the hands of technical experts, has produced a relatively effective method of administration and has assured the public of a better qualified practitioner.

Along with these great reforms have arisen certain social problems. There has been some justifiable criticism of methods used in selecting students. The medical profession has recognized this danger and has spent much time attempting to keep its selection methods adequate. In outlining prescribed courses there has been a tendency to regiment students into a single groove. While there is an appreciable measure of accuracy in the Moss aptitude tests, there is still a large group inside as well as outside the medical profession which is skeptical of excluding men from medical colleges on the basis of this test. In addition to being excluded on the basis of ability, potential candidates have been turned away from medical schools because equipment is not adequate to handle more. The associations have frequently sought to remedy this by reducing the number of students rather than by attempting to secure funds with which to buy equipment. Some have indicated that these barriers were intended to limit the supply of professional men. Oversupply, however, is not entirely due to overcrowding but rather to an abnormal underconsumption. The average well trained medical man is too busy. Most professional men would be delighted to divide their work, but they are not willing to divide their pay. It would seem logical to spend additional effort in making possible the consumption of professional services rather than in curtailing the supply.

When one extends this picture of professional licensure to other professional groups there is created a social system in which ambitious and qualified youth are unable to find intellectual employment. They become discouraged and disillusioned. These rejected medical candidates—some 5,000 to 6,000 annually—constitute a strong nucleus for reform. They maintain that if present day society cannot absorb them, then society must be changed. The more disillusioned youth are turned away, the sooner will follow the organization of some political movement which promises radical changes to assure them of a right to live and work. The American professional associations might ward off this crisis to some degree by several weapons. In the first place there can be the continued improvement of the educational program along lines which will produce the best possible professional men and at the same time assure the greatest degree of fairness to all classes and minority groups. Second, there might be an extension of a system of professional scholarships whereby persons who are capable may enter a field regardless of their economic status. Third, rather than further limit the supply of professional men there could be an increasing emphasis on discovering new needs for professional services. Fourth, the associations could help break down the ridiculous "white collar complex" by which Americans feel that life is a failure unless they are members of a professional class. Society generally needs farmers, coal miners, milkmen, cooks and scrubwomen just as badly as it needs doctors. The professional man will be expected to adjust educational philosophies and policies in order to produce a different interpretation of values.

Another social problem arising from this system of monopolistic licensure is that of making professional services available to those persons who desire them. The masses would like to have these services but cannot pay for them. The public is inclined to hold associations responsible for this situation. To say that the American medical profession has done better at supplying its service than the medical groups of any other country does not answer the question. It so happens that American standards of living generally are higher than those of most European countries. Most Americans admit that medical science has developed to perhaps a higher level in this country than in any other country. They recognize that the American medical profession has done much to relieve suffering, but they also feel that present facilities could provide much more service than is now being given.

The Advisory Council on Medical Education

DR. WILLARD C. RAPPLEYE, New York: The Advisory Council on Medical Education was created to meet the need of a central agency to help coordinate the efforts of various organizations concerned with the different phases of medical education. Since its organization the Advisory Council has been studying three phases of medical education: college preparation for professional study, the internship, and interstate endorsement of licensure. Students are preparing for medical studies in about 800 different colleges and universities. These institutions are baffled by the wide variations in the requirements of different medical schools. As a true success of a physician is determined by his character, personality, industry, initiative, resourcefulness and judgment quite as much as by his technical knowledge, the selection of students for medical study should be based on these qualities.

The college period should be devoted to general rather than largely scientific education. The only college subjects in which every medical student needs some basic knowledge are chemistry, biology and physics. They serve as an introduction to scientific methods and thought and, when well presented, provide the elementary tools of objective, quantitative study now so important in every medical field.

Recognizing the widening public, cultural and educational interests of medicine, the Advisory Council on Medical Education recommends to the Association of American Medical Colleges, the Association of American Universities and the Association of American Colleges that the college preparation for medical studies above the necessary grasp of the fundamental principles of biology, physics and chemistry should be

devoted to general education rather than additional forms of preprofessional education.

The problems of the internship have been studied by numerous bodies in recent years. There is a growing disposition to regard this period of hospital training as a part of the basic medical training and as such to place on medical faculties cooperating with the hospitals a larger responsibility for the guidance and approval of that hospital experience. The relationship of the internship to licensure is of great importance. A few states have adopted regulations which seriously hamper the development of a sound educational program in the internship. A number of questions related to this problem need to be explored. As the internship is now universally regarded as a part of the basic preparation for the practice of medicine, the Advisory Council on Medical Education recommends to the Federation of State Medical Boards that an internship of not less than twelve months and of satisfactory educational content be required for admission to the state licensing board examinations in all states.

The new Advisory Council on Medical Education is dedicated to the sole purposes of preserving and promoting adequate standards of medical education at its several levels through helping to bring about cooperation among existing organizations and agencies. It is endeavoring to bring about integration of the entire program of medical education in this country by common action through "peaceful persuasion in a reasonable manner."

DISCUSSION

DR. WALTER L. BIERRING, Des Moines, Iowa: We should remember, from what Dr. Pratt said, that the committee now in charge of the distribution of refugee physicians is different from the committees that were formed earlier, when racial characteristics evidently prevailed. I join in his appeal for a more charitable interpretation of the citizenship clause; perhaps some form of temporary license or probation period should be granted to a refugee physician so as to determine his fitness. There is reason to look on the situation in a little different light now from that of some years ago. I agree that the state licensing boards should have better control or at least should be more generally interested in the intern service and that there should be some standard of general intern service that can be approved by all boards. If the principle of reciprocity or interstate endorsement is to prevail, it should be on the basis of the certifying examination. No matter if the examination is the equivalent, is as exhaustive and as comprehensive as the examination required by the act prevailing in the state, there should be no difficulty at this time, when medical training has reached that more or less uniform stage, of bringing about interstate endorsement.

DR. I. D. METZGER, Pittsburgh: I want to speak a word in respect to the émigré. Our experience has been that many of these people are not so desirable as they have been shown by recommendations and other means. They have been trained in an entirely different atmosphere from ours, in most cases at least. They have been aggressive, most of them, in social lines and therefore have adopted ideas which to me do not necessarily tend toward the best type of social life in our country. To bring them here and expect them suddenly to adapt themselves to the needs of American medicine is more than we can ask. The same thing would apply if we went abroad. We would have difficulty in adapting ourselves to their social situations, and we would have great difficulty in securing a license in any of those countries. The statement was made that the purpose is to distribute these people to the country districts which are not supplied with physicians. The fact of the matter is that in our state you can't drive them into the country districts. They want to be associated with their own groups of foreign people, who are assembled in the cities and not in the country districts. Let these people stand on the same basis as American physicians. Let them comply with the qualifications required by the law, without any deviation. If you evaluate their premedical college work you can't get more than one year of premedical work out of their credentials. How we can accept that when we have two years' requirement I don't know, yet we are doing it. We require also that these must be signed by the dean, approved by the minister of state in the country in which they have been received, and viséed by the American consul in that district. We do not accept student books which they carry around and which are subject to alteration. We found three persons who had all sorts of credentials, but because of our intern year we required them to go into the hospital and they did not know the first thing about medicine. They are more bewildered in the hospital than our own boys are, very often, in coming out of medical school, and patients resent their presence.

DR. THOMAS J. CROWE, Dallas, Texas: Every one of our medical colleges is turning away every year from 500 to 1,500 applicants for entrance. Notwithstanding that they have the premedical qualifications, only a limited number of students can be admitted. What are we going to do with them? The question is whether or not we owe anything to our own young men, whether or not we shall import the émigrés and deny our own young men entrance to our medical colleges. I hear a lot about the rural communities being without physicians. What is the real situation in Texas, and I presume it is the same throughout the United States? We have in Texas over 300 hospitals. We have 254 counties. Farmer Jones puts the madam in a limousine and goes off to the hospital. When the boy is smashed up in his roadster on the highway does he call the rural doctor? No, he runs the boy to the city hospital. There isn't any rural community in medicine in the United States any more.

MR. WILLIAM C. MACTAVISH, New York: I would like to make a strong plea for liberal, sympathetic and fair consideration of this refugee problem by the state boards. These refugees have been admitted to this country after careful scrutiny by our immigration authorities and they come on the same footing as any other people who intend to become citizens of our country. In most cases I think the level of character among this particular group is at least as high as most of the immigrants we get. Men trained in other professions or trades who come to this country are permitted to earn their living here, using the same profession they had on the other side. In medicine it is somewhat different, but we can safeguard that by requiring them to take the same rigid examinations to which our own graduates are exposed. At present, because of the laws, it is possible for them to settle in only a limited number of states. It would be desirable if they were allowed to spread out over the country. The number is very small and they will be absorbed within a short time. Many of them are highly qualified. They would be desirable acquisitions in any community. I have had occasion to meet several of them. It has been remarkable for me to see a man in his late fifties, with a limited knowledge of English, within a short time learn enough English to take examinations and also to pass these examinations. How many of us who have been out of medical school twenty or twenty-five years could now pass the examinations in the preclinical subjects? I don't say they should be given any special consideration whatever, but they should be given a fair chance, treated as any other immigrants. As for the number who may be undesirable, I think the percentage would be found to be the same or even less than in any other group.

DR. JULIAN F. DUBOIS, St. Paul: In 1912 Dr. Bevan reviewed American medical schools and informed us that we were graduating too many doctors and advised the schools to curtail their enrolment or increase their requirements to prevent overcrowding. That was largely done, and thousands of American boys have been prevented from taking medical courses, and I assume it is the same in other professions. Now we are confronted by a people who have had a catastrophe. In spite of the fact that we have prevented our own boys from taking this work, we are now advised to take what is comparatively a large group. If there are places where there is a scarcity of physicians, we in Minnesota do not know it. Have we a moral right to give away the birthright of the oncoming student? Dr. Bierring's subject to me is the open field of the future. He is not advising that we take all the people from South America, Mexico and so on but that we begin to establish relations, which I think is the coming field. I am gratified to hear Dr. Rappleye's report. The classification of hospitals that we have had in the past, as being good for interns, is largely a myth. I have interviewed students taking the examination, regarding their internship, and with many of them I think the best that you could say was

that they had a fair place to live, perhaps only a fair table and, if they had a lot of energy, they could get some material; but the hospital and the staff did nothing for them.

DR. N. B. BUIE, Marlin, Texas: There has been a lot said about these immigrant physicians. We have a country of great resources. We can't license old physicians. They don't know anything about the things taught in medical colleges today. They want us to examine them on some little trick in public health or surgery, just one thing. They say "This examination is for students, not for us. We are trained physicians." Under the Texas law every fellow gets a number. I don't know whom I am examining. The law says I must not try to find out until after the examination is over. The only way I can tell if a fellow doesn't belong here is when I can't read his writing. They try to describe everything you ask on the liver and heart in a few lines and then have the United States Senator write you a letter. I want to say what the doctor from the state of Pennsylvania said. Our first duty is to our own boys. I like every one. We can't let them come in because we are sorry for them. In Texas we have some of the refugee physicians. We licensed a few of them before we changed our law. Every one of them, unless he has an uncle with a big store, is starving in the practice of medicine. Dr. Rappleye certainly rang the bell. There is no attempt at teaching in the majority of hospitals of this country. When an intern comes out he knows less medicine than he did when he graduated. It is ridiculous. Uniformity of teaching in the hospital is just as important as it is to regulate the teaching in the medical school. We can tell hospitals what they should do to get good interns and they will do it.

DR. W. D. JOHNSON, Batavia, N. Y.: It seems that New York has been the mecca of the refugee. Dr. Pratt told us that 125 men had been placed by his committee in New York largely in rural communities where they need doctors. I come from a rural community. I know at least a half dozen that have been, we realize, planted in our western New York communities. Apparently towns from 5,000 to 20,000 have been selected as places for the refugee physician. I know the medical situation in every one of these towns. Not one of them needed any more doctors than they had. I don't think there is a great deal to this refugee physician problem that we need worry about. If I have any indictment of refugee physicians it is because they do not furnish good enough competition for our young men who are coming out of medical colleges to be a stimulus, and we need that stimulus. They are city people; they don't belong in a rural community at all. The men that I know are good men and they will make good citizens.

DR. EDWARD A. KNOWLTON, Holyoke, Mass.: We have taken a liberal hospitality in Massachusetts toward the refugees. Some of our board members have not been of that opinion, but I have. I have been very glad to welcome good doctors to our state. I think most of these refugees are competent to practice medicine. About denying the privilege to the home boy, and all that, I think we are shedding crocodile tears because most of those fellows who have applied to medical school have been rejected by the school as not proper persons to go into the medical schools. About credentials, which the doctor from Pennsylvania brought up, we realize they can't get their credentials certified by people in Europe now. We have adopted the principle that if a man comes in with his student books, which usually cover at least five years of medical study, and with a license to practice in Germany, we accept him for examination. We have questioned once in a while whether or not the papers were fraudulent but we have a couple of very good men in Boston, Dr. Soma Weiss and Dr. Tannhauser (he is over at Tufts), who know conditions in Germany and know medical education, and we can simply ask them to see whether or not these credentials are valid or fraudulent, and we have gone by their opinion. We haven't run across any crooks.

DR. R. G. LELAND, Chicago: It seems to me we ought to be gratified over the discussion which was brought by Dr. De Lancy on the relations of the social sciences to medicine. It is necessary, however, in any consideration of the effect of the social sciences or social conditions on the distribution of medical services, the practice of medicine or the licensure for medical practice, to consider certain other features which I believe the medical profession deserves to have said about it. The medical profession of this country would dislike any sort of legislative or regulatory system which would mean the placing of physicians in a particular place in any part of the country. Those who have spoken have illustrated the difficulties which have confronted many physicians in recent years in retaining a rural practice. Physicians have frequently found, after a considerable time of devoted service to the rural people, that their rural clients were going to the cities for medical services and later the doctors were compelled to seek other fields. Improved roads have made it possible for medical services to be distributed more easily and farther than at any other previous time. I dislike to believe that the people of this country are denied medical services because they have no money with which to pay. The best information that we can get is to the effect that people of this country are not denied medical care if they have the knowledge of the places to go to get it and if they have the desire for medical care. We must remember that 10 per cent or more of the population do not want medical care. The question of distribution of medical services is complicated, one in which we need the help of all those who have something to offer, the economists, the social scientists and others. But to lay at the feet of the medical profession the responsibility of deciding and finding a solution to all of these problems is unfair. One of the greatest problems today is to put to work the 9,000,000 unemployed people; when those people are employed, many of the problems confronting medicine in the distribution of its services will have been solved overnight. It ought to be recognized also that medicine has done more than many of the other scientific groups to attempt the solution of this problem. It has today performed many more experiments in the methods of giving people good medical service for the amounts that they can afford to pay than all of the other groups combined have ever done. Therefore it is necessary to withhold judgment for a time as to the progress and the methods which should be used. The medical profession is attempting to the best of its ability to find means whereby good medical care can be made available easily and at reasonable prices for all people in the United States. The medical profession must continue to exhibit a sympathetic interest in and the same kind of devotion to the sick people of this country, practicing good medicine as physicians have always done in the United States. If we will continue a sustained effort in this direction, trying the best we can to find a pattern that will safeguard not only the kind of medical care that is given the sick people but the kind of training that is necessary for the physicians who are to follow, the future of medicine will be safeguarded. We must never lose sight of the future of medicine. We should avoid those methods and those efforts which, although they may seem to offer certain solutions for the exigencies of the time, will in all probability be a detriment or a hindrance to the generations of men and women in the future who safeguard the lives of the people.

DR. JOSEPH H. PRATT: I have always thought we could learn a good deal from the German medicine of the good old days. When I was put in charge of a clinic in 1927 I had no money with which to secure as assistants American physicians, but I was able, by making a trip to Germany, to get three German physicians, assistants of well known masters there, to come on fellowships. I thought and still think that it is a broadening association to have men working elbow to elbow who have had a different type of education. From 1927 until the present time I have always had German physicans on my staff. At present I have a staff in the clinic of about thirty-five doctors, nine of whom have degrees from German universities, and all have done and are doing excellent work.

FRANCES P. DE LANCY, PH.D., Morgantown, W. Va.: I should like to remind you that you are not only members of the medical profession but also citizens and voting citizens and consequently interested in the total welfare of the United States. I think it is a wrong attitude for the medical profession to feel that it stands on one side of the fence with the public on the other side and that there is some kind of a fight going on. It should be a picture of cooperation, which was the theme that I was trying to make this morning.

FEBRUARY 13—AFTERNOON

Relationship Between Advertising and the Practice of Medicine

DR. K. E. MILLER, Washington, D. C.: Such knowledge as physicians may have about governmental regulations concerning foods, drugs, cosmetics and devices is largely confined to the activities of the Food and Drug Administration. These pertain to what the labels say about the quality, quantity and value of a product. The measures employed to induce persons to buy these products constitute advertising. It is a function of the Federal Trade Commission to require that advertising be fair and truthful. The Wheeler-Lea Amendment enacted in 1938 defines false advertising.

The Federal Trade Commission cannot stop the sale of any product because of false advertising, nor is it endowed with authority to impose punitive penalties. Its maximum corrective power in such circumstances is the issuance of a cease and desist order specifying claims and inferences in advertising which are adjudged to be false and misleading after weighing all the evidence bearing on the subject. The cease and desist order also demands the discontinuance of the specific claims, or others of like import.

The present law with respect to false advertising of foods, drugs, cosmetics and devices is reasonably adequate to deal with most of the abuses in this field. There is good advertising and bad advertising. The former has a vital and necessary part to play in our economic life and welfare. The latter is an outlaw against which the hand of the law and the bans of decency are raised. There is an ever increasing urge from within the drug industry itself for more conservative and reliable advertising. Any honest advertising may be assured of no difficulties at the hands of the Federal Trade Commission. On the other hand, false and fraudulent advertising may expect no quarter. No fair minded advertiser could find fault with this policy.

The great bulk of the Federal Trade Commission's problems with respect to drugs has to do with preparations sold to the lay public for self medication. Whether we like it or not, self medication is the inalienable right of Americans, and it is here to stay. The question confronting the medical profession is what attitude we shall take toward the problem. I will not attempt either to justify or to condemn self medication. Certainly the hazards would be much less if, along with a conservative recital of the virtues that might be anticipated, the purchaser of home remedies were told the unvarnished truth as to their therapeutic limitations. If persons are going to buy medicines for self administration, as is inevitable, then in the interests of life saving, to which all upright physicians must be committed, they should be served with reliable information on which to base mature judgment. This having been done, the individual becomes solely responsible for any evil consequences. The Federal Trade Commission has undertaken to enforce truthfulness in advertising of drugs and allied products in order to safeguard the public. Incredible as it may seem, the files of the Federal Trade Commission are replete with letters from physicians attesting the virtues of all grades of proprietary remedies. There is no nostrum so rank as to be unable to secure endorsement by some one authorized to affix an M.D. to his name. A more serious embarrassment arises from medical authorities whose published statements are either too old or too new. In the former classification are many erroneous conceptions that have been carried forward from medical antiquity and incorporated in recently published textbooks. At the other extreme are the new and unproved ideas of recognized leaders in contemporary medicine. There is another side of the picture which much more truly characterizes the medical profession. The true spirit of the medical profession is portrayed in that class of men who have on numerous occasions given unsparingly of their time and talent to render medical testimony, without compensation, when called on to do so by the Federal Trade Commission. Among these unsung heroes, not a few have been known to refuse fancy fees for testimony contrary to their convictions, preferring instead to testify for the government along the lines which they knew to be scientifically honest. The Federal Trade Commission is proud to acknowledge the valiant support it has unfailingly received from the medical profession in the investigation of its most difficult and important cases.

Philosophic Trends in Medical Practice Laws

DR. H. M. PLATTER, Columbus, Ohio: Almost fifty years has elapsed since medical practice acts were enacted and the responsibility of administration of them was lodged with boards of licensure in the several states. The purposes of these enactments were to increase the educational qualifications of practitioners and to protect the public from incompetents and charlatans. Today the licensing bodies are further apart than several years ago, and apparently each state is developing an individuality of procedure. As a result, so-called reciprocity is outmoded and endorsement has taken its place. Recent decisions of the Supreme Court of the United States as well as the decisions of the district and state courts seem to legalize more and more the acts of administrative boards. Laws providing for annual registration, basic science and lay administration have also been enacted in several of the states.

That the United States, as a whole, might be benefited by the adoption of a uniform medical practice act might be taken for granted if the machinery for enforcement could be made possible; but without amendment to the federal constitution such procedure cannot be undertaken. In the absence of it the interested bodies should meet in frequent conference to determine how best to proceed to improve present day administration. Broadly speaking, such procedure will quite likely carry us further than the enactment of new laws, for as I interpret present day trends the authority granted us is susceptible of great extension and can easily be modified by the adoption of additional requirements without the enactment of new laws which might need to be amended or repealed.

If it should finally be determined that boards of licensure can exercise more power by the adoption of board resolutions, we ask your aid to see that it is wisely used. In this manner our efficiency can be increased, particularly with the cooperation of the profession, health authorities and others. A sentiment for law observance and law enforcement must prevail in a community to accomplish results worth while. Strong trends to individual action should not complicate friendly relations with other states, and conferences with other agencies can develop a better understanding of our duties and obligations.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, April 13, page 1485.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II, June 17-19. Part III, June or July, to be given in medical centers having five or more candidates desiring to take the examination. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. *Oral.* Part II. New York, June 10-11. Applications must be received 60 days prior to examination. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGOY: November 1940. *If a sufficient number of applications were received before March 1 an examination will be held at New York, June 10-14.* Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* In advance of the meeting of the American Medical Association. Applications must be on file six weeks in advance. *Written.* October 21. Applications must be on file by September 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *General oral and pathologic examinations (Part II), (Group B)* will be conducted in Atlantic City, N. J., June 7-10. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* New York, June 8-10; Cleveland, Oct. 5. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF OTOLARYNGOLOGY: New York, June 3-5. Sec., Dr. W. P. Wherry, 1509 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PATHOLOGY: New York, June 10-11. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: Memphis, Tenn., Nov. 17, preceding the annual meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Cincinnati, May 17-18. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: New York, June 7-10. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., Rochester, Minn.

AMERICAN BOARD OF SURGERY: St. Louis. Part II, April 27. Sec., Dr. J. Stewart Rodman, 225 South Fifteenth St., Philadelphia.

Book Notices

War Wounds and Air Raid Casualties. Articles Republished from the British Medical Journal. Foreword by Sir William P. MacArthur, K.C.B., D.S.O., M.D. Cloth. Price, 10s. 6d. Pp. 256, with 11 illustrations. London: H. K. Lewis & Co., Ltd., 1939.

This is a series of twenty-three pertinent articles by authoritative writers republished from the *British Medical Journal*, with a foreword by W. P. MacArthur, Lieutenant General, Director General, British Army Medical Service. Chapters are devoted to the discussion of injuries of the head, chest, abdomen, genito-urinary tract, extremities, and peripheral nerve and blood vessels. Other chapters cover the subjects of shock, transfusions, amputations, chemical warfare, air raid precautions, effects of high explosives, and psychologic emergencies during war. The text is given largely to consideration of the treatment of the types of casualties noted. Discussions of medical field service and the organization of aid posts and hospitals are also included. It will be readily understood that only the most essential facts can be recorded in a book of such small volume. It is unhesitatingly recommended for the reader who desires a brief but authoritative discussion of the conditions which the medical officer will meet in active service.

A History of Tropical Medicine Based on the Fitzpatrick Lectures Delivered Before the Royal College of Physicians of London 1937-38. By H. Harold Scott, C.M.G., M.D., F.R.C.P., Director, Bureau of Hygiene and Tropical Diseases, London. In Two Volumes. Cloth. Price, $12.50 per set. Pp. 648; 649-1165, with 13 plates. Baltimore: William Wood & Company, 1939.

This is precisely the sort of a book to be expected from a British scholar familiar with colonial administration and accustomed to a wide horizon and a long view of the world and men with the diseases which afflict them. It is scholarly, comprehensive without being loaded with insignificant detail, remarkably free from support of controversial subjects, and adhering closely to the theme. Perhaps quite naturally the data from British imperial sources are more fully presented than those from others contributory to the field. Moreover, the author is a realist and is keenly aware of the distinction between the discovery of a scientific basis for the control of a disease and the practical results of its use. Thus he says of malaria "In malaria, with the discovery of the parasite, its mode of development and its transmission, we thought we had gone far; when it was found that one genus only of mosquitoes, Anopheles, would transmit infection, we congratulated ourselves that now we had the key to eradication of malaria. We were wrong; that was only a half-way step. We have known it now for nearly forty years, yet malaria in warm climates is as bad, as rife, as prevalent as ever, and nearly as fatal as it was a quarter of a century ago."

He notes the difference between tropical medicine, on which there are many treatises, and its history, of which there is none, but only casual scattered comments. The very definition of tropical medicine is elusive; the tropics of Cancer and Capricorn do not delimit it; "diseases in warm climates" include the whole of medicine. "Prevailing diseases in the tropics" fail to account for recorded changes in incidence. For instance, malaria, cholera, plague, hookworm, leprosy, smallpox and typhoid, once regarded as tropical in origin, are in reality quite as much endemic in temperate regions. Some diseases are, however, confined to the tropics because their vectors occur there, such as trypanosomiasis and others of parasitic origin. The author includes Rocky Mountain fever in this list, evidently unaware of the geographic location of Bitter Root Valley!

He cuts the Gordian knot by resolving not to write a history of tropical diseases but of tropical medicine. Quite naturally he begins the story with chapters on the British navy and mercantile marine and turns next to the army and then to the colonies, protectorates and dominions, to India and Australasia, for a historical survey of the conflict with disease in these far-flung outposts of empire.

The major part of the two large volumes is given to a historical account of the diseases customarily regarded as tropical, to wit malaria, blackwater fever, yellow fever, African and American trypanosomiases, the leishmaniases, leprosy, cholera, plague, undulant and relapsing fevers, melioidosis, dengue, amebic dysentery and hepatitis, ancylostomiasis and the avitaminoses, such as beriberi, epidemic dropsy, pellagra and scurvy, and diseases due to akee and ginger poisoning, and their treatments. Two chapters are devoted to the Suez and Panama canals and the part they played in the fight against tropical diseases, and one to the slave trade and the part it played in the distribution of tropical diseases and the continuing problems of the Negro and his diseases.

A closing section is devoted to the lives of Jacobus Bontius, David Bruce, James Carroll, Oswaldo Cruz, John Everett Dutton, Juan Carlos Finlay, Garcia da Orta, William Crawford Gorgas, Jesse W. Lazear, William Boog Leishman, James Lind, Patrick Manson, Hideyo Noguchi, Walter Reed and Ronald Ross, with portraits. There is a bibliography of significant items and very full indexes of names and subjects.

This book ought to be in every medical library, and every medical student should read it to give him a perspective in time and space of the worldwide and age old sway of human disease, largely as yet unchecked in some fields but with increasing promise of prevention and control in others. It is full of dramatic interest to every physician.

Die Tuberkelbacilluria: ihr Wesen und ihre klinische Bedeutung. Von Dr. Karl Breu, Tuberkulosefürsorgearzt beim Staatl. Gesundheitsamt Ludwigsburg. Nr. 74, Tuberkulose-Bibliothek: Beihefte zur Zeitschrift für Tuberkulose. Herausgegeben von Dr. Franz Redeker, Oberregierungs- u. Obermedizinalrat, Berlin, und Dr. Karl Diehl, Dirigierender Arzt, Sommerfeld. Paper. Price, 3.50 marks. Pp. 31. Leipzig: Johann Ambrosius Barth, 1939.

This monograph (or reprint) in German from the *Zeitschrift für Tuberkulose* records the author's opinions and observations on tubercle bacilluria, with briefs of twenty-three cases. According to Breu, who expresses the Dimtza view, tubercle bacilluria is a condition in which tubercle bacilli are passed into the urine in cases of extrarenal tuberculosis (1) through healthy kidneys, (2) through nontuberculous but otherwise altered kidneys and (3) through altered kidneys in the sense of a so-called nephritis tuberculosa. The essential literature is reviewed, beginning with the observations of Foulerton and Hillier in 1901. Various phases are discussed leading to the view of Uebelhör and Schneider that (1) the determination of tubercle bacilli in the urine does not indicate the existence of a urogenital tuberculosis and justify nephrectomy, (2) to exclude a surgical kidney tuberculosis, exact urologic examinations are necessary, and (3) in each case of tubercle bacilluria a sufficiently long observation period is essential to determine the presence of an organic operable renal tuberculosis. Breu reports that in the twenty-three cases of open pulmonary tuberculosis he was able to obtain animal pathogenic tubercle bacilli from the urine without the slightest proof of the existence of a renal tuberculosis. The still prevalent view that the determination of tubercle bacilli in the urine leads to a diagnosis of an operable renal tuberculosis is not substantiated here. The tubercle bacilluria is viewed as an index of a general disease injury, a generality problem of the tuberculous condition. Two pages of references are appended. This monograph will interest primarily the investigator or specialist who reads scientific German. It is flavored mainly with German speaking literature and views but is well printed and readable.

Fruit and Vegetable Juices. By Donald K. Tressler, Ph.D., Head, Division of Chemistry, New York State (Geneva) Agricultural Experiment Station, Maynard A. Joslyn, M.S., Ph.D., Assistant Professor of Fruit Technology, University of California, Berkeley, and George L. Marsh, M.S., Associate, California Agricultural Experiment Station, Berkeley, California. Cloth. Price, $6 domestic; $6.25 foreign. Pp. 549, with 80 illustrations. New York: Avi Publishing Company, Inc., 1939.

This is an authoritative discussion of the preparation and preservation of fruit and vegetable juices for high nutritive value and palatability. The first section is devoted to the history and future of the juice industry. Prior to 1925 the only preserved juice of any commercial importance was bottled grape juice. Canned grapefruit juice was first prepared on a commercial scale in 1926, tomato juice in 1928, pineapple juice in 1931 and orange juice in 1934. Since 1935 the production of canned juices has approximately doubled and the authors predict that the industry will continue to grow at least as long as better and better products are offered. Then follow sections that include an outline of the principles of preparation and preservation of juices, brief but adequate descriptions of the

more important types of equipment now available, designs of plant layouts for the efficient operation and production of high quality juices, tested laboratory methods for preparing and preserving the lesser known juices, and methods of utilizing fruit juice concentrates, syrups, beverages and wastes. Of more general interest is the section dealing with the nutritive values of fruit and vegetable juices. It is difficult for any one not familiar with the scientific literature on nutrition to obtain any definite information on the amounts of the several vitamins actually found in fresh and preserved fruit and vegetable juices. In this volume are tables showing not only the composition of all fruits and vegetables used for juice but also the most recent data on their vitamin content. At the end of each chapter is an excellent bibliography. There is an appendix that includes extracts of recent federal and state legislation relative to the fruit and vegetable juice industry and a subject index. The book is well written, well illustrated and timely. It merits the careful consideration of all persons engaged in the juice industry, dietetians and nutritionists.

Fever and Psychoses: A Study of the Literature and Current Opinion on the Effects of Fever on Certain Psychoses and Epilepsy. By Gladys C. Terry, Research Associate in Neurology, Neurological Institute of New York, Columbia University. Cloth. Price, $3. Pp. 167. New York & London: Paul B. Hoeber, Inc., 1939.

The author has collected and summarized the published data and personal opinions of clinicians concerning the effect of fever on various psychoses. The fever treatment of psychoses resulting from syphilis or its complications has purposely been omitted from the volume. The monograph first describes the clinical effects of intercurrent natural fevers on functional psychoses and epilepsy. It then summarizes the results of artificially induced fevers in the affective psychoses, schizophrenic psychoses and epilepsy. The references to the literature are copious and extend back to the middle of the nineteenth century. The book is well organized and presents the subject clearly. It draws no false conclusions from the mass of often very contradictory material. On finishing the book the reader will come to the author's conclusion that the wide divergence of expressed opinions is evidence, in itself, of the fact that the subject of febrile influences on the so-called functional psychoses is essentially a matter of speculation largely determined by background and bias. Because of the critical unbiased manner in which the material has been collected and presented, the volume is of great use to the student and physician interested in the subject. There is an excellent bibliography but no index.

Traité d'ophtalmologie. Publié sous les auspices de la Société française d'ophtalmologie par MM. P. Bailliart, Ch. Coutela, E. Redslob et E. Velter, René Onfray; Secrétaire général. Tome VI: Pathologie (fin); Neurologie (début). Par MM. J. Coppez et al. Cloth. Price, 400 francs. Pp. 954, with illustrations. Paris: Masson & Cie, 1939.

The sixth volume of the new French encyclopedia of ophthalmology appears according to the time schedule originally outlined. The format is the same as that of the previous volumes except that a slightly better grade of paper has been used. The contents and authors are: Diseases of the Vitreous by Koby, of Paris; Congenital Disorders of the Eyeball by Coppez, of Paris; Ocular Injuries by Danis, of Brussels; Burns of the Eyeball by Coppez; Panophthalmitis and Sympathetic Ophthalmia by Coppez; Pathologic Tension by Magitot, of Paris; Diseases of the Orbit by Terrien, of Paris; Cranio-Orbitofacial Malformations by Patry, of Geneva; Relationship of Ocular Disease to Diseases of the Ear, Sinus, Throat and Teeth by Worms, of Lyons; Introduction to Ocular Neurology by Tournay, of Paris; Diseases and Traumas of the Optic Nerve by Gabriel and Gilbert Sourdille, of Nantes; Tumors of the Optic Nerve by Nordman, of Strasbourg; Diseases of the Chiasm by Hartman (roentgenologist) and David, of Paris; Diseases of the Retrochiasmal Optic Pathways by Monburn, of Paris, and Ophthalmic Migraine by Jean-Gallois, of Paris. Koby's chapter on the vitreous is excellent and is well illustrated, particularly from the standpoint of biomicroscopy. Although many of the other chapters are good, both in scope and in detail, there is on the whole somewhat of a feeling of disappointment in that the detailed management of individual phases is not quite up to what one expects in such a monumental work. Apart from Koby's chapter and the two chapters by the Sourdilles, the illustrations are somewhat sparse and inadequate. But the greatest disappointment of the entire volume is the chapter on glaucoma by Magitot, which is more fitted for a textbook on ophthalmology than for an ophthalmic encyclopedia. However, the final chapter, on ophthalmic migraine, fairly sparkles in its brilliance.

Reihenmässige Röntgenuntersuchungen der in der Kinderfürsorge und -pflege tätigen Berufsgruppen. Von Dr. C. L. Paul Trüb, Regierungs- und Medizinalrat, Berlin. Nr. 76. Tuberkulose-Bibliothek: Beihefte zur Zeitschrift für Tuberkulose. Herausgegeben von Dr. Franz Redeker, Oberregierungs- u. Obermedizinalrat, Berlin, und Dr. Karl Diehl, Dirigierender Arzt, Sommerfeld. Paper. Price, 5.40 marks. Pp. 40. Leipzig: Johann Ambrosius Barth, 1940.

This small volume (actually a bound monograph) of a statistical study by clinical and roentgenologic means of certain regulated groups (nurseries, orphanages, schools) in Arnsberg, Westphalia, should prove of value to all interested in tuberculosis health hazards and public health in general. A clinical-roentgenologic examination is urged for all employees in the care of nurslings, small children, school children and youths. A yearly examination roentgenologically is advised. When active tuberculosis is found, the occupation is discontinued until activity has subsided. With well grounded suspicion of tuberculosis, or when inactive tuberculosis is present, a greater supervision with frequent clinical-roentgenologic control examinations is to be pursued. Those employed in nurseries or schools having charge of children should be given cards recording the results of examination and are transferred with each change of location. The monograph is well written and contains a bibliography of ninety-three references to the subject at hand. The tabulations will prove of interest in noting the details of such a survey and in percentage figures based on the types of tuberculous disease found. The monograph is well worth the nominal price if one is interested in the particular problem considered by the author. It is not a textbook but a specialized monograph of group statistics in tuberculosis dealing particularly with children and those having charge of them.

Plumbism and Chronic Nephritis in Young People in Queensland. By R. Elliott Murray, M.B., B.Sc., D.T.M. Together with a Method for the Estimation of Lead in Biological Materials. By R. Elliott Murray and I. F. Stephens. Service Publication Number 2 (School of Public Health and Tropical Medicine, University of Sydney). Commonwealth of Australia, Department of Health. Paper. Pp. 119, with illustrations. Sydney, 1939.

Chronic nephritis in Queensland, Australia, and especially Brisbane is unduly prevalent as a factor in mortality in age groups under 30 years. This investigation, issued under the authority of the Minister for Health, implicates lead intoxication in children as the most likely cause rather than scarlet fever, focal sepsis, mosquito-borne diseases and climatic effects. The source of the lead is thought to be weathered and powdered house paint. The technic and advantages of the diphenylthiocarbazone (dithizone) method for the estimation of lead in biologic material is incorporated in the study.

Facts and Theories of Psychoanalysis. By Ives Hendrick, M.D. Second edition. Cloth. Price, $3. Pp. 369. New York: Alfred A. Knopf, 1939.

The first edition of this volume appeared in 1934. The present edition gives a brief description of psychoanalysis with reference also to its technic. Some of the sections have been rewritten to agree with studies published within the past five years. Two new chapters concern psychologic study of organic disease and the application of psychoanalysis to conditions other than medical. The author is one of the few writers in this field who seems to be capable of addressing himself understandably to a lay audience.

The Hospital Care of Neurosurgical Patients. By Wallace B. Hamby, M.D., F.A.C.S., Associate Professor of Neurology, University of Buffalo School of Medicine, Buffalo. Cloth. Price, $2. Pp. 118, with 24 illustrations. Springfield, Illinois, & Baltimore: Charles C. Thomas, Publisher, 1940.

Here is a book well conceived, clearly written and concise, which achieves admirably the purpose for which it was designed. It was prepared for the information of resident house officers and nurses as to their duties to patients suffering from the common neurosurgical diseases, both before and after operation. It is not to be supposed, however, that no others will benefit

by its perusal. The author has the happy faculty of presenting in a readily understandable form all that is material without obscuring the presentation with unnecessary detail. He is also to be complimented on the clear and truly illustrative line drawings, which are apparently his own handiwork. There are a few minor errors and possible omissions. The most accessible vein for venoclysis at the ankle is situated just lateral and anterior to the internal malleolus, not medial and anterior to the external malleolus (pp. 43 and 45). In the presence of an intraspinal tumor the spinal fluid may be yellow and contain an excess of protein above as well as below the "block" (pp. 29-30). Somewhat more detail as to (1) the contraindications to and dangers from lumbar and cisternal puncture (pp. 23-29) and (2) the treatment of "shock" (p. 55) might be desirable. However, these are all matters of little consequence which do not detract from the value of this excellent small monograph. There is an extensive index but no reference to the literature.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Practice of Chiropractic by Podiatrist.—The petitioner was licensed to practice chiropractic in Maryland and in New Jersey, in which latter state he had an office. In New York he was licensed to practice podiatry, and the present proceeding arose in that state. After a hearing on a charge of practicing medicine without a license, the state board of podiatry examiners recommended that the petitioner's license to practice podiatry be suspended for one year. The board of regents, however, revoked the license, and the petitioner applied to the supreme court of New York, appellate division, third department, for a reversal of the revocation order.

The evidence against the petitioner consisted of the testimony of three women investigators from the department of education. The petitioner admitted that he examined these women and that he gave spinal adjustments to one of them. There was evidence that he gave to one of the investigators certain pamphlets discussing chiropractic treatments and various subjects relative to health, and that he also gave her a card bearing his name, followed by the abbreviation Ph.C., which he said meant Philosopher of Chiropractic. In defense of his actions, the petitioner testified that he was much interested in chiropractic from a scientific standpoint and that he had attended chiropractic schools, including a New York school of chiropractic from which he received a diploma. He admitted that he had "adjusted" a few relatives and charity patients but contended that, except with respect to the persons acting as investigators for the department, he had not otherwise transgressed the law.

Technically, said the court, the acts admitted by the petitioner constituted the practice of medicine and the engaging in a practice beyond the privileges and rights accorded to him as a podiatrist. The court did not think, however, that it had been established satisfactorily that the petitioner had engaged in the practice of medicine or had violated the terms and conditions of the act under which he was licensed as a podiatrist, according to ordinary meaning and understanding; the instances of violation were too few, casual and trivial. In the face of a penalty so drastic, namely, the revocation of the license, the court thought that justice required that there be proof of more flagrant violation of the law than the isolated and technical instances shown. The order of revocation was accordingly annulled and the case remitted for further hearing.

In a dissenting opinion, Justice Bliss said in part:

> The evidence against petitioner was all furnished by paid women investigators of the Department of Education who went to him and asked for treatment. The Board of Podiatry Examiners, which heard the charges against the petitioner, has found that he questioned one of these investigators concerning her general physical condition, required her to disrobe, used upon her neck and back an apparatus allegedly for the examination of nerves, pressed, manipulated and prodded her back and spine, twisted her neck, jerked her head from side to side, pressed upon her forehead, said that her trouble was pressure on the nerves and a general, rundown condition, that she would need at least ten treatments at $5 each, advised her to have X-ray photographs taken of her whole spine, lateral and cervical, so that he could work properly and give her better results, described the condition of her spine and said that he could cure hay fever with his treatments; took her blood pressure with the use of an instrument and said that it was a little low, but not bad, listened to her chest wall with a stethoscope and said that her heart was good, took her pulse, examined the mark of an incision on her abdomen and said that an ovary had not been removed, that his treatments would relieve pressure on the spine which was the cause of hay fever, that after a few treatments he would bring the blood pressure up to normal. He told her she had arthritis and two bad curvatures of the spine and that her left hip was higher than her right. As to the other investigator, he questioned her concerning her general physical condition, felt of her spine, feet and ankles, said that the muscles of the calf of her left leg were strained, pressed, manipulated and prodded her back and spine, twisted her neck, jerked her head from side to side, jerked her left shoulder, leg and foot and manipulated her feet, told her there was pressure on her sciatic nerve and that such pressure caused pain and that he could cure her and that she needed five or six of his treatments at $5 each.
>
> This dissenting justice found it difficult to understand what more the petitioner could have done had he been a fully licensed doctor of medicine. Under the guise of a podiatrist, this justice said, the petitioner assumed to practice medicine. Justice Bliss, therefore, dissented from the majority opinion and voted to confirm the revocation order.—*Application of Merendino (N. Y.), 10 N. Y. S. (2d) 800.*

Dental Practice Acts: Advertising as Constituting Dishonorable Conduct.—In separate proceedings the district court of Wyandotte County, Kan., enjoined the State Board of Dental Examiners of Kansas from enforcing orders it had entered revoking the licenses of the plaintiffs to practice dentistry, and the board appealed to the Supreme Court of Kansas where the cases were, in effect, consolidated.

The dental practice act of Kansas authorizes the board of dental examiners to revoke licenses "if issued to the individuals who have by false or fraudulent representations obtained or sought to obtain said license or money or any other thing of value or have practiced under names other than their own, *or for any other dishonorable conduct.*" Prior to the institution of the revocation proceedings, both the dentists advertised in certain newspapers in Kansas City, Kan., and both dentists maintained either on the outside of the buildings in which their respective offices were located, or in the entry ways thereto, display cases containing specimens of dental work. In 1937 the Kansas dental practice act was amended, making it unlawful for dentists to advertise in certain designated ways "or to employ 'cappers' or 'steerers' to obtain patronage or to exhibit or use specimens of dental work, posters, or any other media calling attention to the public to any person engaged in the practice of dentistry." After the enactment of this law both dentists made efforts to comply with it. Their advertising copy was revised and the advertising manager of one of the newspapers running their advertisements was advised by the attorneys for the newspaper and by the office of the attorney general of Kansas that the revised copy complied with the law. Apparently the board received similar advice from the attorney general's office. Before the revised advertising copy of the accused dentists was published the advertising manager wrote to the president of the dental board informing him of the advice received from the attorney general's office and submitted the proposed advertising for an opinion by the board. The president of the board promised a definite answer within a week but the only answer ever given was the commencement of revocation proceedings.

After hearings, the board found that since the defendants admitted that they advertised as noted and maintained display cases of dental work "they were therefore guilty of practicing dentistry in an unlawful manner and contrary to the laws of the state of Kansas." In the opinion of the Supreme Court, the board of examiners could revoke a license only for one or more of the causes set out in the dental practice act. The only possible ground for revocation in these cases was that the conduct of the dentists constituted dishonorable conduct, since advertising per se was not named in the act as a ground. The fundamental issue involved, said the court, was whether or not the revocation orders were unreasonable, arbitrary or oppressive under the facts. The 1937 amendment to the dental practice act had not been judicially interpreted, the court pointed

out, but the dentists made efforts to revise their advertising to comply with the new law after obtaining legal advice. An effort was made, too, to have the board pass on the propriety of the proposed advertising. After revocation proceedings were instituted the dentists discontinued all advertising and the use of display cases, informing the board that, notwithstanding the legal advice they had received, they would make every effort to comply with the law as interpreted by the board. When the dentists ceased such advertising, in an effort to comply with the personal views of the members of the board, it was no longer necessary, the court said, to revoke their licenses in order to protect the public against what the board conceived to constitute infraction of a criminal law. The board nowhere made a specific finding that the dentists were guilty of dishonorable conduct but proceeded on the theory that any act which in its opinion violated the 1937 amendment constituted grounds for the revocation of a license regardless of any and all extenuating circumstances. In the opinion of the court, the action of the board was unreasonable and resulted in an arbitrary and oppressive judgment.

While the findings of an administrative agency are not open to review or interference by the courts except where fraudulent, arbitrary or in excess of its authority, and while courts are not permitted to substitute their judgment for that of administrative tribunals, yet courts are definitely charged with the duty of determining whether the procedure employed in reaching that judgment or whether the judgment itself, as rendered, is unreasonable, arbitrary or oppressive, under the circumstances of each particular case. An administrative body cannot be the final judge of the reasonableness of its own orders. An administrative body has wide discretion in determining its judgments, but the discretion cannot be abused; it must actually be exercised reasonably in view of all and not merely some of the circumstances involved.

The board contended finally that its orders of revocation should be sustained irrespective of the 1937 advertising law. It was argued that there was before the board evidence that advertising had been taught to be unethical in the dental school which one of the dentists attended, that advertising was regarded as unethical by the profession and that advertising therefore constituted dishonorable conduct. Many wholesome philosophies and doctrines are taught in the professional schools, said the court, which professional societies are eager to adopt but which they have not yet been able to persuade their members to adopt as a part of a code of ethics. There was nothing in the record to indicate, the court pointed out, that the state dental society had adopted a code of ethics prohibiting the kind of advertising employed in these cases or any other kind of advertising. Whether or not the violation of a professional code of ethics constitutes dishonorable conduct was not before the court. The board of dental examiners made certain specific findings, but it did not find that the dentists in question were guilty of dishonorable conduct. If such a finding was intended, the court thought, it could not be sustained.

The judgments of the trial court enjoining the enforcement of the orders of revocation were therefore affirmed.—*Capland v. Board of Dental Examiners; Brown v. Same (Kan.), 87 P. (2d) 597.*

Society Proceedings

COMING MEETINGS

American Medical Association, New York, June 10-14. Dr. Olin West, 535 N. Dearborn St., Chicago, Secretary.

Academy of Physical Medicine, Richmond, Va., Apr. 24-26. Dr. Herman A. Osgood, 144 Commonwealth Ave., Boston, Secretary.

American Association for the Surgery of Trauma, Atlantic City, N. J., June 7-8. Dr. Ralph G. Carothers, 409 Broadway, Cincinnati, Secretary.

American Association for Thoracic Surgery, Cleveland, June 6-8. Dr. Richard H. Meade Jr., 2116 Pine St., Philadelphia, Secretary.

American Association of the History of Medicine, Atlantic City, N. J., May 4-5. Dr. Henry E. Sigerist, 1900 East Monument St., Baltimore, Secretary.

American Association on Mental Deficiency, Atlantic City, N. J., May 22-26. Dr. E. Arthur Whitney, Washington Road, Elwyn, Pa., Secretary.

American Broncho-Esophagological Association, New York, June 5. Dr. Paul Holinger, 1150 N. State St., Chicago, Secretary.

American College of Chest Physicians, New York, June 8-10. Dr. Robert B. Homan Jr., P. O. Box 1069, El Paso, Texas, Secretary.

American College of Radiology, New York, June 12. Mr. M. F. Cahal, 540 North Michigan Bvld., Chicago, Executive Secretary.

American Gastro-Enterological Association, Atlantic City, N. J., June 10-11. Dr. Albert F. R. Andresen, 88 Sixth Ave., Brooklyn, N. Y., Secretary.

American Heart Association, New York, June 7-8. Dr. Howard B. Sprague, 50 West 50th St., New York, Secretary.

American Laryngological Association, Rye, N. Y., May 27-29. Dr. C. J. Imperatori, 108 East 38th St., New York, Secretary.

American Laryngological, Rhinological and Otological Society, New York, June 6-8. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

American Neurological Association, Rye, N. Y., June 5-7. Dr. Henry A. Riley, 117 East 72d St., New York, Secretary.

American Ophthalmological Society, Hot Springs, Va., June 3-5. Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn., Secretary.

American Orthopedic Association, Kansas City, Mo., May 6-9. Dr. Ralph K. Ghormley, 110 Second Ave. S.W., Rochester, Minn. Secretary.

American Otological Society, Rye, N. Y., May 30-31. Dr. Isidore Friesner, 36 East 73d St., New York, Secretary Pro-Tem.

American Pediatric Society, Skytop, Pa., May 2-4. Dr. Hugh McCulloch, 325 North Euclid Ave., St. Louis, Secretary.

American Proctologic Society, Richmond, Va., June 9-11. Dr. Curtice Rosser, 710 Medical Arts Bldg., Dallas, Texas, Secretary.

American Psychiatric Association, Cincinnati, May 20-24. Dr. Arthur H. Ruggles, 305 Blackstone Blvd., Providence, R. I., Secretary.

American Radium Society, New York, June 10-11. Dr. William E. Costolow, 1407 South Hope St., Los Angeles, Secretary.

American Society for Clinical Investigation, Atlantic City, N. J., May 6. Dr. Eugene M. Landis, University of Virginia Hospital, Charlottesville, Va., Secretary.

American Society of Clinical Pathologists, New York, June 6-10. Dr. Alfred S. Giordano, 531 N. Main St., South Bend, Ind., Secretary.

American Surgical Association, St. Louis, May 1-3. Dr. Charles G. Mixter, 319 Longwood Ave., Boston, Secretary.

American Therapeutic Society, New York, June 7-8. Dr. Oscar B. Hunter, 1835 Eye St. N.W., Washington, D. C., Secretary.

Association for the Study of Internal Secretions, New York, June 10-11. Dr. E. Kost Shelton, 921 Westwood Blvd., Los Angeles, Secretary.

Association of American Physicians, Atlantic City, N. J., May 7-8. Dr. Hugh J. Morgan, Vanderbilt University Hospital, Nashville, Tenn., Secretary.

California Medical Association, Coronado, May 6-9. Dr. George H. Kress, 450 Sutter St., San Francisco, Secretary.

Connecticut State Medical Society, Hartford, May 22-23. Dr. Creighton Barker, 258 Church St., New Haven, Secretary.

Florida Medical Association, Tampa, Apr. 29-May 1. Dr. Shaler Richardson, 111 West Adams St., Jacksonville, Secretary.

Georgia, Medical Association of, Savannah, Apr. 23-26. Dr. Edgar D. Shanks, 478 Peachtree St. N.E., Atlanta, Secretary.

Illinois State Medical Society, Peoria, May 21-23. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

Iowa State Medical Society, Des Moines, May 1-3. Dr. R. L. Parker, 3510 Sixth Ave., Des Moines, Secretary.

Kansas Medical Society, Wichita, May 13-16. Mr. Clarence G. Munns, 112 West Sixth St., Topeka, Executive Secretary.

Louisiana State Medical Society, New Orleans, Apr. 22-24. Dr. P. T. Talbot, 1430 Tulane Ave., New Orleans, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, Apr. 23-24. Dr. Richard T. Shackelford, 1211 Cathedral St., Baltimore, Secretary.

Massachusetts Medical Society, Boston, May 21-22. Dr. Alexander S. Begg, 8 Fenway, Boston, Secretary.

Minnesota State Medical Association, Rochester, Apr. 22-24. Dr. B. B. Souster, 493 Lowry Medical Arts Building, St. Paul, Secretary.

Mississippi State Medical Association, Jackson, May 14-16. Dr. T. M. Dye, McWilliams Bldg., Clarksdale, Secretary.

Missouri State Medical Association, Joplin, Apr. 30-May 1. Mr. E. H. Bartelsmeyer, 634 North Grand Blvd., St. Louis, Executive Secretary.

National Gastroenterological Association, New York, June 4-6. Dr. G. Randolph Manning, Room 319, 1819 Broadway, New York, Secretary.

National Tuberculosis Association, Cleveland, June 3-6. Dr. Charles J. Hatfield, 50 West 50th St., New York, Secretary.

Nebraska State Medical Association, Omaha, Apr. 22-25. Dr. R. B. Adams, 416 Federal Securities Building, Lincoln, Secretary.

New Hampshire Medical Society, Manchester, May 14-15. Dr. Carleton R. Metcalf, 5 South State St., Concord, Secretary.

New Jersey, Medical Society of, Atlantic City, June 4-6. Dr. Alfred Stahl, 55 Lincoln Park, Newark, Secretary.

New Mexico Medical Society, Albuquerque, May 27-29. Dr. L. B. Cohenour, 219 West Central Ave., Albuquerque, Secretary.

New York, Medical Society of the State of, New York, May 6-9. Dr. Peter Irving, 2 East 103d St., New York, Secretary.

New York State Association of Public Health Laboratories, Rochester, May 20. Miss Mary B. Kirkbride, New Scotland Ave., Albany, Secretary.

North Carolina, Medical Society of the State of, Pinehurst, May 13-15. Dr. T. W. M. Long, 321 Hamilton St., Roanoke Rapids, Secretary.

North Dakota State Medical Association, Minot, May 6-8. Dr. Albert W. Skelsey, 20½ North Broadway, Fargo, Secretary.

Ohio State Medical Association, Cincinnati, May 14-16. Mr. C. S. Nelson, 79 East State St., Columbus, Executive Secretary.

Oklahoma State Medical Association, Tulsa, May 6-8. Dr. L. S. Willour, 210 Plaza Court Bldg., Oklahoma City, Secretary.

Rhode Island Medical Society, Providence, June 5-6. Dr. Guy W. Wells, 124 Waterman St., Providence, Secretary.

Society for the Study of Asthma and Allied Conditions, Atlantic City, N. J., May 4. Dr. W. C. Spain, 116 East 53d St., New York, Secretary.

Society of Surgeons of New Jersey, Paterson, May 22. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.

South Carolina Medical Association, Charleston, Apr. 30-May 2. Dr. E. A. Hines, Seneca, Secretary.

South Dakota State Medical Association, Watertown, May 20-22. Dr. Clarence E. Sherwood, Madison, Secretary.

Texas, State Medical Association of, Dallas, May 13-16. Dr. Holman Taylor, 1404 West El Paso St., Fort Worth, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

1: 245-292 (Feb.) 1940

*Disruption of Postoperative Abdominal Wounds. J. M. Donald, Birmingham.—p. 245.
Intra-Ocular New Growths. E. N. DeWitt, Bridgeport, Conn.—p. 250.
History of Urology in Alabama. J. U. Reaves, Mobile.—p. 258.
Brief Review of Pathology of Endometrium. L. C. Posey, Birmingham.—p. 267.

Disruption of Postoperative Abdominal Wounds.—Donald analyzes twenty-seven cases of wound disruption that occurred at the Hillman Hospital during the last five years and five seen in private practice. The twenty-seven disruptions were encountered in 5,603 consecutive laparotomies, an incidence of 0.53 per cent. This figure probably does not represent the true incidence, as the cases are not all properly recorded. This is especially true of cases of incomplete disruption and those treated by strapping and not by secondary closure. Many hernias, not explained on the basis of gross infection, may be the result of unrecognized incomplete disruption. The incidence of disruption is probably higher than is generally recorded. Upper abdominal incisions disrupted in fifteen, or 47 per cent, of the group, midabdominal in six, or 19 per cent, and low abdominal in eleven cases, or 34 per cent. The greatest number of disruptions occurred in the winter months, suggesting the importance of respiratory infections and cough as an etiologic factor. Excessive intra-abdominal pressure, whether from cough, vomiting, distention or undue activity of the patient, appears to be the most important cause. Faulty or too quickly absorbable suture material, infection, hematoma, allergy and poor healing power of the tissues are thought to be secondary factors. Close observation of the wound will enable one to recognize disruption before it is complete and to institute proper treatment. Conservative treatment by strapping rather than a routine immediate secondary closure is recommended. The mortality rate in the author's series was 28 per cent; 33 per cent following secondary closure and 10 per cent following conservative treatment by strapping.

American Journal of Diseases of Children, Chicago

59: 459-692 (March) 1940

*Life Histories of Ninety-Five Children with Chronic Ulcerative Colitis: Statistical Study Based on Comparison with a Whole Group of 871 Patients. R. J. Jackman, J. A. Bargen and H. F. Helmholz, Rochester, Minn.—p. 459.
Disseminated Giant Cell Reaction: Possible Prodrome of Measles. W. A. Stryker, Chicago.—p. 468.
Studies in Immunity: VI. Correlation of Reaction to Schick Test and Diphtheria Antitoxin Content of Blood Serum in Children with Scarlet Fever. C. E. Duffy and A. G. Mitchell, Cincinnati.—p. 479.
Effects of Natural and Refined Sugars on Oral Lactobacilli and Caries Among Primitive Eskimos. D. B. Waugh and L. M. Waugh, with technical assistance of Marjorie P. Waugh, New York.—p. 483.
Enuresis in Neglected Children. E. Wexberg, New Orleans.—p. 490.
*Treatment of Pneumonia by Sulfapyridine and by Hydroxyethylapocupreine Dihydrochloride. Maud L. Menten, R. R. Macdonald and Natalie Brönykovsky, Pittsburgh.—p. 497.
Etiologic Studies of Sporadic Cases of Encephalitis Occurring in the St. Louis Area in 1938. Margaret G. Smith, E. H. Lennette and R. J. Blattner, St. Louis.—p. 509.
Treatment of Pertussis with Detoxified Antigen. N. M. Greenstein and W. Levy, New York.—p. 515.
Cerebral Sclerosis. A. B. Baker and L. S. Gerber, Minneapolis.—p. 522.
Basal Metabolism of Tuberculous Children: V. Tuberculous Pleurisy. Anne Topper and H. S. Rubin, New York.—p. 535.
Dextrose Tolerance Tests of the Newborn. Rose C. Ketteringham, Cleveland.—p. 542.
Neoplasms Producing Endocrine Disturbances in Childhood. R. E. Gross, Boston.—p. 579.

Life Histories of Children with Colitis.—Jackman and his colleagues have determined statistically the difference between the nature and the course of chronic ulcerative colitis of a group of ninety-five children less than 16 years of age and of a group of 871 patients (children and adults), in which the ninety-five child patients were found. The 871 consecutive patients with the disease came to the Mayo Clinic between 1925 and 1931 inclusive. In the group of ninety-five patients who were less than 16 years old the disease was more common among boys (fifty-seven) than among girls. In the entire group there were 491 male and 380 female patients. There was a gradual increase in the number of patients who acquired the disease as the ages progress through to the age of 15. Approximately two thirds of the children experienced the onset of the disease after 9 years of age. The curve for the age incidence of all the patients suggests that the peak occurs during the late twenties, with a progressive decline as patients approach old age. The majority of patients dated the onset as well as the relapses of the disease as occurring during the months in which infections of the upper part of the respiratory tract are most prevalent. The geographic distribution of the patients was not significant. A majority of the children, as well as the adults, were unable to associate the onset of the disease with any definite predisposing factor. In seventy-three of the children colitis manifested itself in the severe or fulminating form, whereas only 427 of the whole group of patients fell in this classification. Forty-five of the children, or 47.4 per cent, had complicating factors, as compared to 41.3 per cent for the 871 patients. There were 148 deaths during the period of fourteen years among the 871 patients; that is, 17 per cent died before March 1, 1938. Of these, thirteen patients died from causes unrelated to their intestinal disease. Among the ninety-five children twenty-two, or 23.2 per cent, died before March 1, 1938. All these deaths were caused directly or indirectly by the intestinal disease. The average duration of life from the onset of the disease to death was nine years; the shortest period was three months and the longest twenty years. The condition of the patients when last observed was that 11.6 per cent of the children and 19.9 per cent of the whole group were symptom free. Active disease was present in 65.3 per cent of the children and 63.2 per cent of the adult group. Of the children 23.2 per cent were dead, as were 17 per cent of the adult group.

Sulfapyridine and Hydroxyethylapocupreine Dihydrochloride in Pneumonia.—Menten and her associates compare the therapeutic effects on pneumonia of sulfapyridine with those of hydroxyethylapocupreine dihydrochloride and compare both of these with the effects of symptomatic treatment alone. Seventy-nine patients with pneumonia were admitted to the Children's Hospital during the winter of 1938-1939. They were divided into three groups according to the therapy employed. Each group was subdivided into two subgroups, depending on the speed of recovery: 1. The first group consisted of children in whom the infection was apparently due to the pneumococcus alone and there was a speedy, dramatic fall of temperature to normal followed by rapid recovery. 2. In the second group the increased temperature was prolonged for about two weeks and showed wide daily fluctuations (from 99 to 105 F.) regardless of the type of treatment. These patients were toxic and acutely ill. Haemophilus influenzae was frequently cultured from their oropharyngeal swabs, and when these organisms were not obtained the patient's clinical course suggested their presence. Staphylococcus aureus was a secondary invader. A delayed resolution (up to five and six days) in some cases in which the pneumonia was supposedly caused by the pneumococcus alone may have been due to the presence of small numbers of Haemophilus influenzae. Because of mixed infection in some of the cases the authors doubt whether the three deaths in the control group as compared to one death in each of the other groups have much evaluating significance. The computed value of 2.9 days for the average duration of pyrexia before a drop to normal in the drug treated patients, as against 3.2 days for the controls, is likewise of questionable significance. Only the data on the children who responded readily to treatment and had mixed infection are included in this evaluation. In the children who responded to treatment by a fall in temperature within forty-eight hours, crisis was the rule. A decrease in pulse rate paralleled the drop in temperature in most cases, but the pulmonary involvement as indicated by roentgenograms resolved more slowly. Patients whose temperature responded promptly to treatment showed a rapid clinical improvemcnt. This was

most pronounced with the patients receiving sulfapyridine. Nausea and vomiting were frequently observed after the administration of either drug. However, vomiting occurred frequently in children before specific treatment was given and also some of the control group vomited. Prompt relief and return of appetite followed discontinuance of the sulfapyridine. The gastric disturbances, especially among younger children, were more prolonged after the discontinuance of hydroxyethylapocupreine. Cyanosis, restlessness and irritability occurred with the use of sulfapyridine. There was no incidence of jaundice, granulocytopenia or cutaneous rashes. Toxic manifestations of the hydroxyethylapocupreine were confined to gastric symptoms.

American J. Obstetrics and Gynecology, St. Louis

39: 179-364 (Feb.) 1940. Partial Index

Physiology of Anterior Pituitary and Note on Medullotropic Hormone. J. B. Collip, Montreal.—p. 187.
*Blood Lipids in Pregnancy. O. H. Schwarz, S. D. Soule and Bernice Damie, St. Louis.—p. 203.
Vulvovaginal Mycoses in Pregnancy: Relation of Symptoms to Genera and Species of Fungi. B. Carter, C. P. Jones, R. A. Ross and W. L. Thomas, Durham, N. C.—p. 213.
Is There a Clinical Relationship Between Pyelitis of Pregnancy and Preeclamptic Toxemia? R. D. Mussey and S. B. Lovelady, Rochester, Minn.—p. 236.
Rationale for Use of Testosterone Propionate in Immediate Treatment of Excessive Uterine Bleeding. A. R. Abarbanel, New York.—p. 243.
Trachelorlasty (Sturmdorf Technic) in Treatment of Sterility. O. Moore, Charlotte, N. C.—p. 269.
Chemotherapy in Obstetrics and Gynecology. R. G. Douglas, New York. —p. 275.
*Study of Results in 332 Consecutive Cases of Placenta Praevia. I. A. Siegel, Baltimore.—p. 301.
Study of 111 Cystograms for Diagnosis of Placenta Praevia. M. A. Carvalho, Binghamton, N. Y.—p. 306.
*Vaginal Use of Aluminum Hydroxide and Colloidal Kaolin. S. P. Savitz, L. J. Golub and H. A. Shelanski, Philadelphia.—p. 329.
*Use of Testosterone Propionate in Treatment of Menopausal Patient: Preliminary Report on Use of Pellets of Crystalline Testosterone Propionate. D. Silberman, H. M. Radman, Baltimore, and A. R. Abarbanel, New York.—p. 332.

Blood Lipids in Pregnancy.—Schwarz and his associates discuss the changes in blood serum lipid concentration from early pregnancy to term. A lipemia, characterized by a most marked increase in neutral fat and a lesser increment in cholesterol fractions and phospholipid, was observed during pregnancy. The rise in lipid content is gradual throughout the period of gestation. No significant changes in unsaturation of the phospholipid fatty acids or total fatty acids were observed. The ester cholesterol : total cholesterol ratio remained remarkably constant throughout. The phospholipid : total cholesterol ratio exhibited was quite variable but no constant change was noted. No apparent relation to weight gain of the mother or the fetus, hemoconcentration, seminarcosis or anesthesia was observed. A decrease in all lipid elements at delivery was frequent but not constant.

Placenta Praevia.—From an analysis of 332 cases of placenta praevia, treated at the University Hospital from 1920 to 1938 and from 1935 to 1938 at the Baltimore City Hospital, Siegel formulates the following conclusions: 1. The more frequent and liberal use of blood transfusion is paramount in reducing maternal mortality and morbidity. 2. The method of delivery must be determined for each individual case, depending on the type of placenta praevia and the condition of the cervix. 3. Forced delivery, internal version and breech extraction are condemned. 4. The rupture of membranes with or without the use of the Willett clamp will give favorable results in properly selected cases. 5. Cesarean section definitely reduces the maternal and fetal mortality in the central and partial types of placenta praevia and in certain selected cases of marginal placenta praevia. 6. The maternal mortality in the present series was 6.6 per cent in vaginal deliveries and 1.9 per cent in cesarean section deliveries. 7. Deaths of viable babies are greatly reduced by cesarean section.

Aluminum Hydroxide and Colloidal Kaolin for Douching.—Savitz and his collaborators investigated the action of colloidal kaolin and aluminum hydroxide gel when used as a vaginal cleanser in the form of a douche. The patient is instructed to use 15 Gm. of an aluminum hydroxide-colloidal kaolin mixture in 8 ounces (240 cc.) of water. After douching, the patient may use a rinse of several quarts of warm water. If continued action (mucus coagulating effect) is desired, the rinse may be applied several hours later. The douche may be repeated as often as is desired without any harmful effect. The p_H of the mixture is about 7. It supplies neither acid nor alkali to the vaginal tract. It is a neutral, mucus-coagulating, nontoxic, nonirritating substance. If acidity is desired therapeutically, it can be supplied by specific agents. Forty-three patients were given the douche chiefly for vaginal cleanliness, for leukorrhea due to a nonspecific infection in twenty-one (infection due to organisms other than Neisseria gonorrheae, Trichomonas vaginalis and Monilia albicans), for fourteen cases of leukorrhea due to mild cervicitis, for twelve due to Trichomonas vaginalis, for eleven due either to moderate or to marked endocervicitis, for eight due to either moderate or marked exocervicitis, for six cases of salpingitis and for five cases of leukorrhea due to Monilia albicans. The douche has proved a successful cleanser in all these conditions. In trichomonas and monilia cases with marked tenderness, prohibiting immediate treatment, the use of the douche eases the irritation, so that the proper therapeutic measures can be applied. In salpingitis the patient uses 2 ounces (60 Gm.) of the mixture to 2 quarts of hot water every other day for as long as is desired. All the patients showed improvement after the use of this cleansing douche. Toxic or untoward reactions have not been observed.

Testosterone Propionate Implantation for Menopause Symptoms.—From their preliminary studies with the subcutaneous implantation of pellets of crystalline testosterone propionate for menopausal symptoms, Silberman and his colleagues feel that this procedure will eventually supplant the other methods of administering the substance except possibly in mild cases. It has yielded by far the smoothest and most consistent results and from the patients' point of view will prove the most economical one.

American Journal of Ophthalmology, St. Louis

23: 127-244 (Feb.) 1940

Effect of Intravenous Injection of Nonspecific Proteins on Experimental Corneal Ulcers. E. Gallardo and R. Thompson, New York.—p. 127.
Salzmann's Nodular Corneal Dystrophy: Report of Case. E. B. Muir, Salt Lake City.—p. 138.
Syphilitic Primary Optic Atrophy: II. General Considerations and Results of Treatment by Standard Methods, Especially Subdural Treatment and Induced Fever: Critical Review. J. E. Moore and A. C. Woods, Baltimore.—p. 145.
Metastatic Malignant Melanoma of Retina. Ella M. Uhler, Baltimore. —p. 158.
Essential Atrophy of Iris: Pathologic Report. B. Rones, Washington, D. C.—p. 163.
Comparative Study of Benzedrine, Paredrine and Cocaine with Homatropine as Cycloplegics. E. B. Weinman and F. B. Fralick, Ann Arbor, Mich.—p. 172.
Bilateral Plexiform Neuromas of Conjunctiva and Medullated Corneal Nerves: Report of Case. M. P. Kohe and A. E. Braley, Iowa City.— p. 179.
Midline Notching in Normal Field of Vision. H. L. Bair and R. D. Harley, Rochester, Minn.—p. 183.

Archives of Internal Medicine, Chicago

65: 221-464 (Feb.) 1940

*Hypertrophy and Hyperplasia of Islands of Langerhans in Infants Born of Diabetic Mothers. E. B. Helwig, Boston.—p. 221.
Adjustments in Coronary Circulation After Experimental Coronary Occlusion, with Particular Reference to Vascularization of Pericardial Adhesions. H. B. Burchell, Rochester, Minn.—p. 240.
Mechanism of Digitalis Action in Abolishing Heart Failure. H. Gold and M. Cattell, New York.—p. 263.
Comparative Study of Valvular Calcifications in Rheumatic and in Nonrheumatic Heart Disease. B. S. Epstein, Brooklyn.—p. 279.
Electrocardiographic Changes Associated with Pericarditis. P. H. Noth, Detroit, and Arlie R. Barnes, Rochester, Minn.—p. 291.
*Pure Mitral Stenosis in Young Persons. B. J. Walsh, E. F. Bland and T. D. Jones, Boston.—p. 321.
An Acoustical Study of the Stethoscope. F. D. Johnston and E. M. Kline, Ann Arbor, Mich.—p. 328.
Atypical Facial Neuralgia: Diagnosis, Cause and Treatment. M. A. Glaser, Los Angeles.—p. 340.
Gastroscopy and Phytobezoar: Report of Case of Diospyrobezoar. D. C. Browne and G. McHardy, New Orleans.—p. 368.
Renal Calcification Accompanying Pyloric and High Intestinal Obstruction. H. Martz, Brooklyn.—p. 375.
Diseases of Metabolism and Nutrition: Review of Certain Recent Contributions. R. M. Wilder, H. C. Browne and H. R. Butt, Rochester, Minn.—p. 390.

The Pancreas in Infants Born of Diabetic Mothers.—To determine whether an adequate structural basis existed for the assumed hyperinsulinism of infants born of diabetic mothers, Helwig studied the pancreatic islands of nine infants of diabetic and nine infants of normal mothers. Approximately ninety serial

sections from a block of tissue selected at random were cut and stained with phloxine and methylene blue. The glands of the two series were measured and calculated in the same way, making the results reasonably comparable. The islands of Langerhans in the infants of diabetic mothers exhibited a variable degree of hypertrophy and hyperplasia, most marked in those infants nearing full term at birth. The nuclei were frequently enlarged and occasionally hyperchromatic. The stroma and to a less degree the islands were infiltrated with eosinophilic granulocytes, many of which were mature. This infiltration was not present in the control group. One infant in the control group, whose mother was not known to have diabetes, showed hypertrophy and hyperplasia of the islands and no obvious anatomic cause of death. Apparently some infants of diabetic mothers have definitely larger amounts of insular tissue than those of nondiabetic mothers. This is particularly marked in infants whose greater birth weight suggests a possible excess growth stimulus. However, a fair number of the pancreases of infants of diabetic mothers will fall in the normal range of insular size. The determinations of blood sugar on the whole show little correlation with insular size.

Pure Mitral Stenosis in Young Persons.—Walsh and his associates point out that of 1,700 children and adolescents with rheumatic fever observed at the House of the Good Samaritan in Boston since 1920 eighty-one acquired physical signs of so-called pure mitral stenosis. The signs consisted of (1) a low pitched (often coarse) murmur at the cardiac apex, which begins in mid or late diastole and ends with a crescendo in (2) an abrupt, slapping first sound. Changing physical signs in the heart prior to the stage of pure mitral stenosis were observed in forty-eight. These were subdivided into two groups according to the presence or the absence of demonstrable cardiac involvement with the initial attack of rheumatic fever. Twenty-seven patients had auscultatory signs of valvular disease from the onset. In five these signs consisted of a loud, blowing systolic murmur at the apex (mitral regurgitation); in fifteen of a loud systolic murmur and a poorly defined diastolic rumble at the apex; in four of a short, low pitched diastolic murmur after the third heart sound at the apex, without crescendo or accentuation of the first sound and without an accompanying systolic blow, and in three of a slight diastolic blow after the second sound at the base, usually best heard to the left of the upper portion of the sternum and unassociated with murmurs at the apex. A similar murmur was present in fifty-three of the eighty-one cases in addition to the aforementioned signs of involvement of the mitral valve. The second subgroup consisted of twenty-one patients who on recovery from their initial rheumatic fever had no clinical evidence of cardiac involvement —cases of so-called potential rheumatic heart disease. The first evidence of mitral stenosis to appear in two of these was a systolic murmur at the cardiac apex consistent with mitral regurgitation. This progressed slowly to the next stage: apical systolic and diastolic murmurs of mitral regurgitation and stenosis. In three additional cases the latter combination appeared directly as the first indication of heart disease. Later, over a period of years, the systolic murmur gradually became less loud and ultimately disappeared as the diastolic murmur and first heart sound acquired the characteristics of pure stenosis. In the remaining sixteen cases the earliest physical sign to appear was a short mid diastolic murmur following a rather prominent third sound at the apex of the heart. This slight apical diastolic murmur slowly evolved into the characteristic crescendo presystolic murmur of mitral stenosis, unaccompanied by a systolic murmur. In relatively few instances (five) did pure mitral stenosis become established in the first five years after the onset of rheumatic fever. In twenty-seven it developed during the second five years, and in fourteen the characteristic signs did not become established until the third or fourth five years. In two cases the pure mitral stenosis was established more than twenty years after the original illness. The observations are in close agreement with previously recorded postmortem studies, in which it was shown that the ultimate development of extensive valvular deformity of the mitral orifice (either with or without actual stenosis) probably requires a minimum of two years, and in most instances a considerably longer period. The rheumatic fever of the eighty-one patients was characterized by a mild course. In the light of their observations on this deformity the authors believe that the unusually high percentage of older patients with a "negative" rheumatic history is more readily understood. Even in some of their younger patients, under close observation at the time of their active disease, it has been impossible to identify clearly as rheumatic fever their mild illness prior to the appearance of characteristic signs in the heart. It is probable that the favorable course of the illness in the majority of these patients (both young and old) is to be accounted for by the mild rheumatic fever, which in turn favors the continued integrity of the myocardium.

Archives of Physical Therapy, Chicago

21: 65-128 (Feb.) 1940

Backache: Common Causes and Treatment, with Special Reference to Physical Therapy. H. W. Meyerding and G. A. Pollock, Rochester, Minn.—p. 69.
Cross Firing Technic in Short Wave Therapy. P. Bauwens, London, England.—p. 80.
Newer Aspects of Dosage and Technic in Short Wave Diathermy. D. Kobak and E. Mittelmann, Chicago.—p. 87.
Peripheral Vascular Diseases: Diagnosis and Treatment by Passive Vascular Exercises. A. Silverglade, Oakland, Calif.—p. 100.

Canadian Medical Association Journal, Montreal

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Antidiabetogenic Effect of Primary Alcoholic Extract of Pituitary Tissue Administered Orally. J. B. Collip, Montreal.—p. 109.
Interactions Between Various Steroid Hormones. H. Selye, Montreal.—p. 113.
Contribution of Electron Microscope to Medicine: I. Electron Microscope Described. E. F. Burton, J. Hillier and A. Prebus, Toronto.—p. 116.
Sarcoma of Prostate: Report of Case of Rhabdomyosarcoma. H. E. Taylor, Glasgow, Scotland.—p. 120.
Hereditary Jaundice in the Rat. Helga Tait Malloy and L. Lowenstein, Montreal.—p. 122.
Laughlen Test and Blood Donors. P. H. Greey, M. M. Bracken and E. Paul, Toronto.—p. 126.
Rheumatic Heart Disease in Adolescence. R. R. Struthers, Montreal.—p. 128.
The Care of the Premature Child. W. M. Wilson, Windsor, Ont.—p. 133.
*Early Introduction of Solid Foods in Infant Diet. Doris Monypenny, Toronto.—p. 137.
Use of Colloidal Aluminium Hydroxide in Treatment of Peptic Ulcer. J. F. McIntosh and C. G. Sutherland, Montreal.—p. 140.
Dysmenorrhea. E. V. Shute, London, Ont.—p. 145.
Modern Treatment of Nervous Syphilis. A. Marin, Montreal.—p. 152.
Interpretation of Factor of Latency in Syphilis. F. E. Cormia, Montreal, and J. A. Lewis, London, Ont.—p. 154.
Acute Gallbladder: Early versus Late Operation. G. H. Stobie, Belleville, Ont.—p. 158.
Acute Hematogenous Osteomyelitis. R. H. McCoy and D. E. Ross, Montreal.—p. 162.
Clinical Value of Autopsies. R. E. Shaw and W. J. Deadman, Hamilton, Ont.—p. 168.

Early Introduction of Solid Foods to Infant Diets.—Monypenny observed the effects of adding egg, pablum and strained vegetables to the diets of ninety-one infants at the age of 1 month. The majority of these infants were fed artificially from 2 weeks of age and all were artificially fed after 3 months. It was surprising how eagerly some infants, even at 1 month of age, took the first solid feeding. Spoon feeding was established with less difficulty at 1 month of age than at 5 or 6 months. New solids were usually introduced with greater ease at 5 months when spoon feeding had been started at 1 month. Of the seventeen infants placed on egg, only one seemed more contented with egg in the feeding than before, and this infant had loose stools. Diarrhea, vomiting and discomfort occurred following the addition of egg in 41 per cent of the cases and gave the impression that egg added early to the infant's diet should be done with the greatest of caution. The addition of 15 Gm. of dry pablum to the diet of twenty-seven infants improved disturbed stools and in two instances was more effectual than protein milk in correcting the stools. There was no laxative action. Many of the infants seemed more satisfied and slept better. The impression was that pablum could be added to the infant's diet at 1 month of age with safety. Vegetables given at 1 month of age to eighteen infants with normal stools did not cause looseness. When the stools were previously constipated they were improved. No infant having loose stools at 1 month of age was placed in this group. Discomfort did not follow the addition of vegetables, and sometimes the baby seemed more satisfied. Therefore it seemed that vegetables could be safely added at this early age to the diet of infants with previously good stools. The remaining twenty-nine infants served as controls and were fed milk dilutions with no addition of solids.

Journal of Investigative Dermatology, Baltimore

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Hereditary Hypotrichosis in Rat (Mus Norvegicus). E. Roberts, J. H. Quisenberry and L. C. Thomas, Champaign, Ill.—p. 1.
*Metabolic Studies on Patients with Pemphigus. J. H. Talbott, W. F. Lever and W. V. Consolazio, Boston.—p. 31.
Influence of Diets of Varying Fat Content on Experimentally Produced Cutaneous Infections in White Rats. J. L. Callaway and R. O. Noojin, Durham, N. C.—p. 71.

Metabolic Studies on Patients with Pemphigus.—Talbott and his colleagues state that the pathogenesis of pemphigus is intimately connected with one or more metabolic disturbances. Abnormal concentration of the following constituents was found in the serum of ten patients with acute pemphigus: sodium, total fixed base, potassium, protein and nonprotein nitrogen. These concentrations are consistent with acute adrenal insufficiency. An increase in plasma, blood and interstitial fluid volumes was observed in all cases in which there were generalized cutaneous lesions. Five of the patients with acute pemphigus were given supportive or nonspecific treatment only. Death followed in from eleven days to eight weeks after the onset of the acute symptoms. Postmortem examinations were allowed on three. Damage to the adrenal glands was evident in two. The remaining five with acute pemphigus were given large amounts of adrenal cortex extract and sodium chloride solution parenterally. Clinical improvement followed with restoration of the acid-base changes. Two patients have had a remission which has persisted for three and one half and three years respectively, without further treatment. A remission was achieved in the other patients on this regimen but it persisted only as long as active material was administered. Eventually this became ineffective. The changes in the concentration of constituents in the blood of the patients with chronic pemphigus were less constant. The therapeutic data on these patients were not conclusive.

Journal of Lab. and Clinical Medicine, St. Louis

25: 445-556 (Feb.) 1940. Partial Index

Blood Pigments: Properties and Quantitative Determination, with Special Reference to Spectrophotometric Methods. H. O. Michel and J. S. Harris, Durham, N. C.—p. 445.
Relation of Dietary Calcium-Phosphorus Ratio to Iron Assimilation. H. D. Anderson, K. B. McDonough and C. A. Elvehjem, Madison, Wis.—p. 464.
Transfusions and Polycythemia in Normal and Tumor Bearing Rats. F. M. Allen, New York.—p. 471.
Does Hemolytic Streptococcus Infection or Sulfanilamide Affect the Alpha Hemolysin of Serum? Emily May Bixby, Wrentham, Mass.—p. 476.
*Vitamin A Deficiency in Diseases of Liver: Its Detection by Dark Adaptation Method. M. G. Wohl and J. B. Feldman, Philadelphia.—p. 485.
Value of "Repeat" Injection of Tetanus Toxoid (Secondary Stimulus) in Active Immunization Against Tetanus. H. Gold, Chester, Pa.—p. 506.
Histidine Content (Diazo Value) of Blood in Peptic Ulcer. E. G. Schmidt, Baltimore.—p. 512.
Contribution to Question of Determination of Nicotinic Acid in Urine. L. Schindel, Jerusalem, Palestine.—p. 515.
Improved Method for Iodimetric Determination of Pyruvic Acid. G. A. Schrader, Auburn, Ala.—p. 520.
Prothrombin Time Determination. O. R. Kelley and W. E. Bray, Charlottesville, Va.—p. 527.
The Lange Test: II. Influence of Particle Size and Hydrogen Ion Concentration of Gold Sols on Lange Test Readings on Syphilitic and Tabetic Spinal Fluids. P. K. Glasoe and C. H. Sorum, Madison, Wis.—p. 534.
Method of Destroying Blastocysts (Blastocystis Hominis) in Fecal Wet Smears in Order to Facilitate Examination for Endamoeba Histolytica. E. G. Hakansson, Washington, D. C.—p. 546.
Capillary Hematocrit Method of Determining Blood Cell Volume. C. J. Hamre, Honolulu, Territory of Hawaii.—p. 547.

Vitamin A Deficiency in Diseases of Liver.—Wohl and Feldman detected early the occurrence of vitamin A deficiency in twenty-five patients with hepatic disease. In the absence of retinal, choroidal or other ocular pathologic changes a delay in dark adaptation above the normal and specified time is called a functional or latent pathologic dark adaptation and is attributed to avitaminosis A. Ten patients addicted to alcohol, without clinical evidence of hepatic disease, were also examined. In twenty-one of the patients with hepatic disease the dark adaptation time was above normal. These patients showed varying degrees of hepatic damage. Of seven patients with hepatocellular jaundice three presented a normal dark adaptation and a minimal degree of liver damage and four showed evidence of hepatic damage and pathologic dark adaptation. In these four cases the degree of liver damage, as evidenced by the icterus index and other laboratory studies, appeared to run parallel with the dark adaptation. Nine of the ten alcohol addicts showed vitamin A deficiency as revealed by dark adaptation studies. The tenth person, whose dark adaptation was normal, was receiving desiccated thyroid at the time the test was made.

Journal of Neurophysiology, Springfield, Ill.

3: 107-188 (March) 1940

Facilitation and Difficilitation Effected by Nerve Impulses in Peripheral Fibers. J. Erlanger and E. A. Blair, St. Louis.—p. 107.
Human Cortical Area Producing Repetitive Phenomena When Stimulated. R. M. Brickner, New York.—p. 128.
Effects of Eserine, Acetylcholine and Atropine on Electrocorticogram. F. R. Miller, G. W. Stavraky and G. A. Wootton, London, Ont.—p. 131.
Cord Potentials in Spinal Shock: Single Volleys. Winifred B. Stewart, J. Hughes and G. P. McCouch, Philadelphia.—p. 139.
Id.: Multiple Stimuli. J. Hughes, G. P. McCouch and Winifred B. Stewart, Philadelphia.—p. 146.
Id.: Crossed Effects in Monkey Macaca Mulatta. G. P. McCouch, Winifred B. Stewart and J. Hughes, Philadelphia.—p. 151.
Attempt to Produce Sleep by Diencephalic Stimulation. F. Harrison.—p. 156.
Relayed Impulses in Ascending Branches of Dorsal Root Fibers. J. B. Hursh, New York.—p. 166.
Observations on Diaphragmatic Sensation. J. C. Hinsey and R. A. Phillips, New York, with report of case by W. K. Livingston, Portland, Ore.—p. 175.
Phasic Response to Cortical Stimulation. C. G. Smith, F. A. Mettler and E. A. Culler, Rochester, N. Y.—p. 182.

Journal of Pediatrics, St. Louis

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*Vitamin A Absorption in Catarrhal Jaundice. B. B. Breese and Augusta B. McCoord, Rochester, N. Y.—p. 139.
Basal Metabolism of Obese Children. N. B. Talbot and J. Worcester, Boston.—p. 146.
Serial Blood Sugar Determinations in Normal Newborn Infants. J. B. McKittrick, Boston.—p. 151.
*Incidence of Skin Eruptions Among Infants and Preschool Children. S. H. Silvers, Brooklyn, and M. Coe, Queens Village, N. Y.—p. 160.
*Use of Convalescent Mumps Serum. G. W. Kutscher Jr., Asheville, N. C.—p. 166.
Vollmer Tuberculin Patch Test: Evaluation of Its Relative Sensitivity. J. G. Hughes, Memphis, Tenn.—p. 171.
Effects on Monkeys of Sulfapyridine in Doses Comparable with Those Used for Infants. J. A. Toomey, H. S. Reichle and W. S. Takacs, Cleveland.—p. 179.
Chronic Gaucher's Disease. H. H. Perlman, Philadelphia.—p. 191.
Congenital Cystic Dilatation of Single Kidney Calix. L. B. Hart, Beckley, W. Va.; E. I. Dukes and R. P. Forbes, Denver.—p. 206.
Thyroid Deficiency in Twins. H. Hosen, Port Arthur, Texas.—p. 210.
Cabinet Cubicle for Infants, Combining Isolation with Control of Temperature and Humidity. C. C. Chapple, Philadelphia.—p. 215.
Psychologic Care of the Preschool Child. Ruth Morris Bakwin and H. Bakwin, New York.—p. 220.

Vitamin A Absorption in Catarrhal Jaundice.—Breese and McCoord found that the absorption of vitamin A was abnormal in diseases of the liver and in celiac disease. A study of twenty-one patients with catarrhal jaundice showed that the first vitamin A absorption test was normal for six. In the remaining children either the vitamin was absorbed poorly or the rise in the blood was found to be much higher than normal. The original test showed an unusually high rise in the vitamin A of the blood in two cases. The first test showed failure of normal absorption in twelve cases; when the test was repeated seven cases returned to normal levels, four showed a rise of vitamin A above normal and one showed improvement but not normal absorption. There was one fatal case in which only one determination of vitamin A was made. This value was low. Ten of fourteen patients tested within nine days of the onset of the disease failed to absorb vitamin A well, whereas, only three of sixteen patients tested at least ten days or more after the onset failed to do so. Eleven of fifteen patients who were tested, while not improving from a clinical standpoint, failed to absorb vitamin A well, whereas such was found in only one of thirteen patients tested while improving. The icteric index did not bear any obvious relation to vitamin A absorption. Severe degrees of hepatic damage, as measured by the bromsulphalein test, were associated in three cases with failure to absorb vitamin A, whereas lesser degrees of damage were not. Patients with low curves who were given bile salts and retested showed improvement in absorption. In most cases this improvement was maintained when the test was repeated again without the use of bile salts.

Cutaneous Eruptions Among Children.—Silvers and Coe determined the incidence of cutaneous eruptions in 1,696 children from 3 or 4 weeks to 6 years of age. The material for the study was obtained from two baby health stations in New York City. The infants were brought in nine or ten times during the first

year and about four times during the second year. The babies were representative of metropolitan New York. All races (18 per cent of the group studied were Negroes) and nationalities were included. Only those children who attended regularly and kept their appointments were included in the study. Among the 1,696 children 349, or 21 per cent, were found to have some cutaneous ailment. Some of the complaints (thirty-five different diagnoses were made) were of fleeting nature, such as miliaria, gluteal dermatitis, papular urticaria or intertriginous eruptions, while others were of a more permanent nature, such as the various forms of nevi, verrucae or seborrheic and infantile eczemas. Of the 825 babies less than 1 year of age, 246 (29.9 per cent) showed cutaneous eruptions. The percentage of eruptions among the Negro children was appreciably lower than among the white ones. The largest group of cutaneous eruptions encountered was the infantile eczema group, which included all stages. Often the same child progressed from the very mild to the severest stages or vice versa. Whenever possible, an attempt was made to correct any errors in the child's nutrition. Rarely was it necessary to withhold any basic food. They tried to limit the child's clothing and bedding to linen and cotton. Their experience has shown that topical applications for the treatment of infantile eczema are not skilfully applied and that the first thought is usually to experiment with dietary regimens, occasionally with disastrous results to the child's development. One should be able to manage the eruption in most cases by local applications. Stopping the use of soap and water and instituting the application of a neutral powder brought a complete cure in the majority of cases of folliculitis with dermatitis of the face. The authors believe that intertriginous erythema and gluteal erythema of Jaquet are different stages of the same eruption. In many of their cases they coexisted, or the gluteal followed the intertriginous erythema. To counteract these eruptions they recommended the earliest possible training of the toilet habit, frequent changes of diapers, rinsing them in boric acid water after washing, application of liberal amounts of a neutral powder to the areas after thorough rinsing off with water of all soap solution, and the elimination of rubber panties. Overdressing infants in too many woolen, silk and rayon clothes is, in their experience, a common cause of many cutaneous eruptions.

Convalescent Mumps Serum.—Kutscher attributes the infection incidence of only 2 per cent of fifty-one boys exposed to mumps as due to the use of from 8 to 10 cc. of convalescent mumps serum. The reported incidence of from 30 to 50 per cent in exposed and susceptible children following exposure to mumps would have put the expectancy of infection between fifteen and twenty-five boys.

Journal of Pharmacology & Exper. Therap., Baltimore

68: 217-300 (Feb.) 1940. Partial Index

Effect of Selenium on Urease and Arginase. C. I. Wright, Washington, D. C.—p. 220.

*Influence of Epinephrine on Shivering and on Metabolism in the Cold. V. E. Hall and P. B. Goldstone, Stanford University, Calif.—p. 247.

Administration of Drugs in Food for Chemotherapy Studies in Mouse Pneumococcic Infections. R. N. Bieter, W. P. Larson, Elizabeth M. Cranston, Minneapolis, and M. Levine, Washington, D. C.—p. 252.

Experimental Studies in Chemotherapy of Pneumococcic Infections, Including Hydroxyethylapocupreine, Sulfapyridine and Certain Other Related Chemical Compounds. M. M. Bracken, J. M. Johnston, Pittsburgh; G. E. Crum, Crafton, Pa.; D. R. Patrick, H. H. Permar and W. W. G. Maclachlan, Pittsburgh.—p. 259.

Dietary Protein and Toxicity of Sodium Selenite in the White Rat. H. B. Lewis, J. Schultz and R. A. Gortner Jr., Ann Arbor, Mich.—p. 292.

Influence of Epinephrine on Shivering and Metabolism.—Hall and Goldstone find that, in cooled pentobarbitalized cats, epinephrine in doses just in excess of the physiologic rate of secretion suppresses shivering and consequently reduces the total metabolism by decreasing the amount of oxygen consumed by this activity. They attribute these effects to a depression, by epinephrine, of the central motor mechanisms involved in shivering.

Kansas Medical Society Journal, Topeka

41: 45-88 (Feb.) 1940

Prognosis in Heart Disease. J. Jensen, St. Louis.—p. 45.

Appendicitis in Children. E. O. Parsons, Kansas City, Mo.—p. 51.

Observations on Eyes During Insulin Shock Treatment. L. S. Powell, Lawrence; M. E. Hyde and J. Russell, Osawatomie.—p. 55.

Bismuth Poisoning from Bismuth (Subnitrate) Given Orally: Report of Case. J. H. Bena, Pittsburg.—p. 60.

Meralgia Paraesthetica Following Chigger Bite. M. A. Walker, Kansas City.—p. 61.

Medical Annals of District of Columbia, Washington

9: 37-70 (Feb.) 1940

*Practical Considerations of Immunity in Syphilis. J. E. Kemp, Chicago.—p. 37.

Nervous and Mental Components of Gastrointestinal Diseases. N. D. C. Lewis, New York.—p. 42.

Hemorrhagic Adnexal Lesions Producing "Acute Abdomen" with Intraperitoneal Hemorrhage. J. K. Cromer, Washington.—p. 48.

Dermatitis from a Sanitary Belt: Report of Case. I. L. Sandler, Washington.—p. 53.

Alcoholism and the Heart. W. M. Yater and J. Wallace, Washington.—p. 54.

Immunity to Syphilis.—The resistance developed to syphilis has, according to Kemp, certain characteristics which distinguish it from resistance developed to other diseases. 1. Time is a prerequisite for its development; that is, immunity does not become evident until the infection has been present for some weeks. 2. Treatment inaugurated before the immune stage is established may abruptly terminate or at least delay its development. Of eighty-one cases of reinfection, 56.8 per cent occurred in individuals treated for their first infection before the forty-sixth day, in 40.7 per cent of those first treated between the forty-sixth and ninety-first day and in only 2.5 per cent of those in whom treatment was not begun until after the ninety-first day. Experimental studies showed that, as in man, the longer the first infection was allowed to continue untreated the less successful were the attempts to implant a second infection. It must not be inferred that late syphilis always confers an immunity to a second infection. 3. The most striking examples that time is necessary for the development of immunity and that treatment of early syphilis terminates or retards its development are those tragic happenings the neurorecurrences. The majority of these episodes follow the same pattern—an individual with early syphilis receives a few treatments and then lapses. Within nine days to two weeks after his last treatment he reappears with multiple or single cranial nerve palsies. The treatment received was sufficient to prevent the development of his own resistance but was insufficient to eradicate the infection in his neuraxis. When, therefore, the spirochetes remultiplied, they encountered a virtually defenseless host bringing about a series of events much more severe than would have been encountered had no treatment been received. The ultimate outcome in cases in which neurorecurrences develop has been reported to be much less favorable than in cases in which clinical neurosyphilis is not so precipitate. 4. There are a certain number of individuals in whom, after the secondary eruption has healed, the disease will remain latent throughout their lives. They develop and maintain a lasting and effective resistance to their infection. In the remaining individuals resistance will terminate with the development of late lesions of the central nervous system, the cardiovascular system, bones, eyes and the like. When this occurs it represents a breakdown in the individual's immunity. The development of the lesion of late syphilis does not indicate a complete breakdown in the individual's resistance, as in the majority of instances only one type of tissue is affected and often this involvement is only partial. This tendency to breakdown is one of the important characteristics of immunity in syphilis. Regarding syphilis of the central nervous system, the immunity which develops after inadequate treatment of early syphilis is inferior to that of untreated syphilis. 6. Different tissues do not share equally in the resistant state. The frequency of neurosyphilis in contrast to the infrequency of syphilis of the stomach, for example, suggests something more than a mere predilection of the spirochete for nervous tissues, particularly since all the tissues are apparently equally involved in the dissemination of the organisms during early infection. 7. The two factors of known importance in influencing the course of the infection are race and sex. In only one important category, that of cardiovascular syphilis, is the defense of the white individual (7.4 per cent) superior to that of the Negro (11.5 per cent). The increased severity of syphilis in men as compared to women is a striking illustration of the ability of the latter to protect themselves against the disease. Approximately 60 per cent more women than men reach a stage of latency in which positive serologic tests are the only evidence of infection. Pregnancy is not the only factor responsible for the milder course of syphilis in women. Recent experimental investigation on rabbits has favorably altered the course of syphilis by the administration of

estrogenic substances. The course of syphilis in castrated female rabbits was more severe than in normal female rabbits. These observations suggest that the female sex hormones may be responsible for the milder course of syphilis in women than in men.

Medicine, Baltimore

19: 1-160 (Feb.) 1940

Tularemia: Summary of Certain Aspects of Disease Including Methods for Early Diagnosis and Results of Serum Treatment in 600 Patients. L. Foshay, Cincinnati.—p. 1.
*Infectious Mononucleosis. A. Bernstein, Baltimore.—p. 85.

Infectious Mononucleosis.—Bernstein considers infectious mononucleosis in the light of the broadened concept which the Paul-Bunnell test has supplied. When the variety of antibodies which may be elicited in the course of infectious mononucleosis is considered, it is plain that the etiologic agent must be rather unique in this respect. If this organism should be of such a character as to serve as the basis of a vaccine, this material might well prove to be an invaluable agent for the purposes of stimulating a broad nonspecific protective response against infections in general. A plea is made for a wider routine performance of the Paul-Bunnell test, not only as a confirmatory procedure in infectious mononucleosis or as one of the diagnostic agglutination tests in instances of "fever of unknown origin," but likewise when the following conditions exist: (1) unexplained lymphocytosis or glandular enlargement, (2) positive agglutination tests (Widal and the like) without cultural confirmation, (3) false positive Wassermann reaction, (4) unexplained acute conditions of the abdomen, (5) enlarged spleen, (6) atypical conjunctivitis or puffy eyelids and (7) apparent cases of catarrhal jaundice, hemorrhagic purpura, Vincent's infection, aphthous stomatitis, benign lymphocytic meningitis and granulocytopenia. By adopting such an attitude of suspicion, further manifestations of infectious mononucleosis will be unearthed and additional clues disclosed pointing toward its etiology. Infectious mononucleosis, glandular fever, monocytic angina and lymphoid cell angina are probably different manifestations of the same disease, the etiology of which is unknown.

Mental Hygiene, Albany, N. Y.

24: 1-176 (Jan.) 1940

How May the Community Utilize Its Gifted Children? H. W. Zorbaugh, New York.—p. 1.
Errors and Problems in Psychiatry. A. Myerson, Boston.—p. 17.
Group Therapy. S. R. Slavson, New York.—p. 36.
Effects of Incarceration on the Adult Criminal as Observed in a Psychiatric Court Clinic. C. B. Thompson, New York.—p. 50.
Social Factors in Delinquency. G. W. Henry and A. A. Gross, New York.—p. 59.
Loving versus Spoiling Children. M. D. Riemer, Brooklyn.—p. 79.
Some Industrial Placements of Women Patients Paroled from State Hospital. Ethel B. Bellsmith, Central Islip, N. Y.—p. 82.
Convergence of Social Work and Psychiatry: Historical Note. A. Deutsch, New York.—p. 92.
College Fraternity and Adjustment. F. G. Livingood, Chestertown, Md.—p. 98.
Sensory Level in Hygienic Integration. J. E. Davis, Perry Point, Md.—p. 107.
Use and Effect of Alcohol in Relation to Alcoholic Mental Disease Before, During and After Prohibition. H. M. Pollock, Albany, N. Y.—p. 112.

New England Journal of Medicine, Boston

222: 247-288 (Feb. 15) 1940

Clinical Measures in Control of Syphilis. R. A. Vonderlehr, Washington, D. C.—p. 247.
Rupture of Retroperitoneal Duodenum: Report of Case. E. J. Ottenheimer, Willimantic, Conn., and R. L. Gilman, Storrs, Conn.—p. 251.
*Factors Influencing Persistent and Recurrent Hyperthyroidism. D. D. Berlin and S. L. Gargill, Boston.—p. 254.
Dental Problems Associated with Pregnancy. C. P. Sheldon, Boston.—p. 260.
*Clinical and Laboratory Study of Incidence of Fungi in Patients with Cutaneous Eruptions. J. G. Downing, Beulah Merrill and D. L. Belding, Boston.—p. 263.
Abdominal Surgery. A. W. Allen, Boston.—p. 266.

Persistent and Recurrent Hyperthyroidism.—According to Berlin and Gargill, the problem of persistent and recurrent thyrotoxicosis following apparently adequate subtotal thyroidectomy has been discussed ever since the surgical treatment of toxic goiter was standardized. Attempts to solve this problem have varied considerably. Some workers, impressed with the fact that toxic goiter is a constitutional disease of unknown etiology, have advocated the treatment of the unique personality of the patient. Crile, who perceives a biologic relation between recurrent thyrotoxicosis, neurocirculatory asthenia and peptic ulcer, has advocated his dekineticizing operation of bilateral denervation of the adrenals. Others conceive the solution of the problem in adequate thyroidectomy. Scott advocates a total thyroidectomy. The authors studied 235 cases of toxic goiter in which operation was performed at the endocrine clinic of the Beth Israel Hospital from 1932 to 1938. The incidence of persistence and recurrence was 5.1 per cent. W. O. and Phebe K. Thompson and A. E. Morris reported an incidence of 19.5 per cent in a similar series of 190 cases. One of the reasons for the low incidence in the authors' series is that a radical subtotal thyroidectomy has been performed in most of the cases. Another factor may be that the majority of cases have not been followed for a sufficiently long time. It is possible that more of these cases will show recurrence at a later date. The factors probably responsible for persistence and recurrence in this series have been found to be an inadequate thyroidectomy, the unique personality and fundamental imbalance of patients with exophthalmic goiter, frequent upper respiratory infections, and psychic trauma from marital infelicity or financial insecurity. No case of either persistent or recurrent thyrotoxicosis has been observed following subtotal thyroidectomy for toxic nodular goiter. Neither the age, the sex, the initial basal metabolic rate nor the degree of response to iodine appeared to have any part in persistence or recurrence of thyrotoxicosis. The symptoms and signs of many patients with persistent or recurrent thyrotoxicosis can be controlled fairly completely by iodine medication, either alone or in combination with roentgen treatment. Nevertheless the ideal treatment for recurrent and persistent thyrotoxicosis, especially when there is marked degeneration of thyroid tissue, is a maximal or total excision of the thyroid remnants. Such a procedure is likely to result in postoperative myxedema, but this can be satisfactorily controlled by thyroid medication. The incidence of permanent postoperative myxedema in this series was only 3.9 per cent, in spite of the fact that most of the patients had radical subtotal thyroidectomies.

Incidence of Fungi in Cutaneous Eruptions.—Downing and his associates state that 476 patients with cutaneous eruptions were examined from July 1, 1938, to July 1, 1939, at the dermatologic clinic of the Boston City Hospital for the presence of fungi. The existence of fungous infection was suspected in most of the cases. Scrapings were taken from the skin not only at the site of the lesion but elsewhere, for example the feet. Direct microscopic examination of the scrapings from the lesions in cover glass mounts with 20 per cent potassium hydroxide and cultures on Sabouraud's medium were made. The cultural methods were the more informative, since they permitted the identification of species as well as of genera. The value of direct microscopic examination was evident in cases of tinea versicolor, since cultivation of the causative organism was unsatisfactory. The results were positive in 179, or 37.6 per cent, of the 476 cases; 73.7 per cent of the total positives were obtained by direct microscopic examination and 78.7 per cent by cultural methods. The relative value of the two methods depends on the genus of fungus concerned. Both should be used in the diagnosis of fungous infections. The percentage of positive results varies with the different diseases. Tinea capitis, tinea circinata and erosio interdigitalis give a high percentage of positives, and dermatophytosis a fair percentage. Contact dermatitis has an extremely low percentage, an observation which proves that secondary infection with fungi is more or less infrequent. The incidence of tinea capitis, most prevalent in children, shows a seasonal variation, with a decline during the summer vacation months. The cases of dermatophytosis decrease during the cold months. The percentage of positive cases is highest in warm weather. The 179 fungi comprised seven genera, of which the three commonest were Microsporon (41.3 per cent), Monilia (21.8 per cent) and Trichophyton (18.5 per cent). The anatomic distribution of the lesions from which fungi were detected was as follows: head, 29 per cent; body, 19 per cent; upper extremities, 26 per cent, and lower extremities, 26 per cent.

Ohio State Medical Journal, Columbus

36: 121-240 (Feb.) 1940

Errors in Roentgen Diagnosis: Part I. Pseudofracture. G. L. Sackett, Cleveland.—p. 137.
Treatment of Pneumonia. J. M. Ruegsegger, Cincinnati.—p. 145.
*Treatment of Juvenile Adiposogenital Dystrophy with Anterior Pituitary Growth Complex. A. Ruppersberg Jr., Columbus.—p. 149.
Diagnosis and Treatment of Nasal Polyp. E. R. Hargett, Springfield.—p. 151.
Successful Case of Hypodermic Hyposensitization to Wheat. S. R. Zoss, Youngstown.—p. 154.
Arachnodactyly: Report of Case Complicating Pregnancy at Term. W. B. Bean and J. G. Fleming, Cincinnati.—p. 155.
Tuberculosis of Chest Wall: Report of Unusual Case. B. B. Larsen and H. A. Williams, Cleveland.—p. 161.
Severe Anemia Associated with Diaphragmatic Hernia. H. S. Schiro and J. E. Benjamin, Cincinnati.—p. 164.
Errors in Diagnosis. H. S. Applebaum, Cleveland.—p. 167.
Differential Diagnosis of Hyperthyroidism. J. L. De Courcy, Cincinnati.—p. 170.
Cesarean Section: Study of 262 Cases from St. Ann's Maternity Hospital, Cleveland, Ohio. P. V. Duffy, Cleveland.—p. 173.
Comparative Study of Serum and Sulfapyridine in Treatment of Lobar Pneumonia. U. G. Mason and J. B. Stocklen, Cleveland.—p. 177.

Anterior Pituitary Complex for Adiposogenital Dystrophy.—The successful treatment of a case of adiposogenital dystrophy in a girl of 6½ years with the anterior pituitary growth complex is reported by Ruppersberg. The child before treatment was begun weighed 85 pounds (38 Kg.) and her height was 44 inches (112 cm.). She was placed on a diet consisting of a total of 940 calories a day. Thyroxine 0.4 mg. and anterior pituitary gland extract 12 grains (0.8 Gm.) were given daily by mouth. In addition she was given 1 cc. of growth complex intramuscularly three times a week. This treatment was rigidly executed for approximately six months, at which time the patient had apparently lost 23 pounds (10 Kg.) and there was a redistribution of the residual obesity. Her speech response was much improved and her disposition markedly more pleasant. Improvement in both mental and muscular activity was observed. Her height had increased a little more than 1½ inches in the six months of treatment. There was no change in the ovarian function of the patient, according to observation of the mammae and external genitalia. The case was one of marked hypopituitarism (juvenile type of Fröhlich's syndrome) associated with hypothyroidism and possibly a parathyroid imbalance. The author warns that after such a diagnosis has been established any medication which might stimulate sex maturity should be avoided. Therefore any preparation containing the gonadotropic factor of the anterior pituitary gland cannot be used, but the "growth complex" may be employed with safety, since it contains a negligible amount of the factor.

Pennsylvania Medical Journal, Harrisburg

43: 593-752 (Feb.) 1940

Unilateral Exophthalmos and Its Surgical Treatment. A. B. Reese, New York.—p. 605.
Use of Hydroxyethylapocupreine in Treatment of Pneumococcic Pneumonia. W. W. G. Maclachlan, Pittsburgh.—p. 612.
Use of Sulfapyridine in Pneumonia. D. S. Pepper, Philadelphia.—p. 615.
Hydronephrosis Secondary to Noncalculous Ureteropelvic Obstruction. W. I. Buchert, Danville.—p. 625.
*New Procedure for Correction of Ureteropelvic Junction Obstruction. J. G. Moore, Pittsburgh.—p. 631.
Use of Walking Caliper in Fractures of Leg. R. E. Brubaker, Danville.—p. 635.
Prophylaxis of Ophthalmia Neonatorum with Silver Acetate. W. F. Hartman, Philadelphia.—p. 639.
Thyrotoxic Reactions Following Major Operations. G. P. Muller and J. M. Surver, Philadelphia.—p. 642.
The Ophthalmologist and the Workmen's Compensation Law. J. H. Delaney, Erie.—p. 645.
State Aid and Purpose of the Campaign Against Syphilis. E. S. Everhart, Harrisburg.—p. 648.
Management of Early Syphilis in Adults. G. J. Busman, Pittsburgh.—p. 651.
Correction of Massive Defects of Both Eyelids. E. B. Spaeth, Philadelphia.—p. 663.
Hormone Diagnosis of Intra-Uterine Fetal Death: Value of Quantitative Serum Prolan Determinations as Diagnostic Procedure. A. E. Rakoff, Philadelphia.—p. 669.
Defective Hearing and Chronic Ear Disease as Revealed by Examination of 47,000 Philadelphia School Children. W. S. Cornell, Philadelphia.—p. 678.

Procedure for Correcting Ureteropelvic Obstruction.—Moore outlines a method for immediate nephrostomy with the continued use of the same tube as an internal support for the ureter. The method, he believes, should encourage prolonged splinting of the ureter after any type of operation on the ureteropelvic junction, since the tube can be retained without disturbing the patient in any way. The procedure was used in five cases in which operation was performed for hydronephrosis. The time elapsed is not sufficient to permit an evaluation of the permanent results, but the feasibility of the method is indicated. The method is as follows: After the lumbar incision is made, the kidney is exposed over its entire surface. The ureteropelvic junction and ureter are examined, and the cause of obstruction is determined and relieved by the correction indicated in the individual case. A curved uterine sound is passed through the incision in the pelvis and then through the lower calix to the capsule which is incised. The tube is telescoped over the sound for a short distance and drawn into the pelvis. It is then passed down the ureter for about 3 or 4 inches, with two or three fenestrations in the portion which will come to lie in the pelvis. The tubing used is No. 12 or 14 French in caliber. The incision in the pelvis is entirely closed with fine chromic catgut. Nephropexy is always done by elevating a small area of the capsule around the tube and suturing it to the lumbar muscles. The lower pole is supported by a gauze drain. The tube is tied to the muscle with chromic catgut and to the skin with silkworm gut. The gauze and tube are taken out through separate openings in the incision. The tube is allowed to drain into a bottle until the patient is ready to get out of bed, between ten and fourteen days after operation, at which time a screw clamp is closed on the tube very close to the skin and all extra tubing is cut away.

Radiology, Syracuse, N. Y.

34: 131-260 (Feb.) 1940

Epiphysial Dysplasia Punctilaris (Stippled Epiphyses): Report of Case Not Associated with Hypothyroidism. J. A. L. McCullough and C. G. Sutherland, Rochester, Minn.—p. 131.
Present Conception of Treatment of Cancer of Larynx. H. Coutard, Chicago.—p. 136.
Surgical Treatment of Cancer of Larynx. J. H. McCready, Pittsburgh.—p. 146.
Variations in Radiation Technic and Biologic Effects in Treatment of Pharyngeal Cancer. H. E. Martin, New York.—p. 149.
Roentgen Therapy in Acute Puerperal Mastitis. J. F. Elward and S. M. Dodek, Washington, D. C.—p. 166.
Accidental Perivascular Injection of Thorotrast: Report of Two Cases. S. E. Ziffren, Iowa City.—p. 171.
Castration of the Female by Irradiation: Results in 334 Patients. W. S. Peck, J. T. McGreer, N. R. Kretzschmar and W. E. Brown, Ann Arbor, Mich.—p. 176.
Two Years' Experience with 400 Kilovolts Constant Potential Deep Therapy. D. Steel, Cleveland.—p. 187.
Therapeutic and Economic Indications for Teleradium and Supervoltage X-Ray Machine. C. D. Lucas, Charlotte, N. C.—p. 193.
Differential Action of X-Rays on Anterior and Posterior Regions of Tubifex Tubifex. H. Branson and H. Kersten, Cincinnati.—p. 200.
*New Approach to Treatment of Certain Bladder Carcinomas. L. S. Goin and E. F. Hoffman, Los Angeles.—p. 205.
Diagnosis of "Basilar Impression." A. Schuller, Vienna, Germany; revised for publication by L. G. Rigler, Minneapolis.—p. 214.
Submucous Lipoma of Large Intestine: Case Report. W. J. Ravenel, Charleston, S. C.—p. 217.
Principles of New Therapy with High Speed Electrons: Preliminary Report. R. Schindler, New York.—p. 222.

New Approach for Treating Bladder Carcinomas.—Because a large percentage of bladder tumors are either far advanced or extensively infiltrated when first seen, Goin and Hoffman believe that coagulation either does not destroy the tumor or causes such great destruction of the surrounding tissue that occlusion of one or both ureters, obstruction of the neck of the bladder or rectovesical or vesicovaginal fistula results. Total excision is likewise a formidable procedure, carrying a high mortality and being technically difficult, as it involves diversion of the urinary stream either to the colon or to the cutaneous surface. For this group of tumors the authors propose marsupialization of the bladder and intense irradiation of the tumor at its site by the contact therapy method. The preliminary operation consists of a midline cystotomy. No roentgen treatment is attempted until the ninth or tenth postoperative day, in order to avoid the placing of any mechanical stress on the newly marsupialized bladder. On the day treatment is begun, the bladder is irrigated with a 1:10,000 solution of potassium permanganate and the Freyer tube is removed from it. The lower part of the abdomen is cleansed and painted with tincture of merthiolate and draped. The x-ray tube is covered with a sterile stockinet so that only its distal end is exposed and a sterile rubber sheath is pulled

over the end of the tube and part of the stockinet. The patient is given evipal intravenously. The tube is inserted in the bladder, its end in contact with the tumor. The dosage has been as high as 2,556 roentgens per treatment with a roentgen afflux of 1,278 per minute; 1 mm. of aluminum added filtration was employed. Treatment is given on alternate days and the total dose has been as high as 30,672 roentgens given over a period of twenty-seven days. No alarming sequelae have been encountered and the radiation reaction consisted only of injection and increased redness. When treatment is concluded the bladder is closed and the patient discharged after the usual postoperative period. Evipal anesthesia need not be used if the patient tolerates mild pain well. Three cases are reported. The authors draw no definite clinical conclusions, as sufficient time has not elapsed to permit evaluation of the method. They believe that in selected cases a great deal more can be offered a patient with a bladder carcinoma from their combined method than either fulguration or cystectomy can offer.

Texas State Journal of Medicine, Fort Worth

35: 663-744 (Feb.) 1940

What Are the Duties and Responsibilities of the General Practitioner in Treatment of Fractures? Unrecognized Fractures. H. R. Owen, Philadelphia.—p. 668.
Gumma of Brain. J. E. Williams, Galveston.—p. 672.
Psychology in Pediatrics. J. Zahorsky, St. Louis.—p. 676.
Psychiatric Contraindications to Surgery. G. F. Witt and T. H. Cheavens, Dallas.—p. 681.
Vaginal Agenesis. A. G. Cowles, San Antonio.—p. 685.
Indications for Treatment of Malpositions of Uterus. W. B. Lasater, Mineral Wells.—p. 689.
Roentgen Therapy of Infections. E. P. Pendergrass and P. J. Hodes, Philadelphia.—p. 693.
Etiology and Treatment of Glaucoma Preceding and Following Cataract Extraction. W. R. Buffington, New Orleans.—p. 700.
Recurrent Vitreous Hemorrhages in Young Adults—Eales Disease. J. F. Schultz, Houston.—p. 705.
The New Deal and the Doctor. W. B. Russ, San Antonio.—p. 708.
History of Administration of the Dallas Venereal Disease Clinic Since Its Reorganization in 1936. J. W. Bass, Dallas.—p. 712.

Virginia Medical Monthly, Richmond

67: 67-130 (Feb.) 1940

The Cancer Problem. M. R. Reid, Cincinnati.—p. 67.
Care of Skin of the New Born: Preliminary Report. J. M. Whitfield and H. W. Farber, Richmond.—p. 75.
Use of Cow Horn Peg in Fractures of Neck of Femur, with Special Reference to Types of Fractures Suitable for Use of the Peg and Method Employed in Introducing Same. P. W. Boyd, Winchester.—p. 77.
Endocrinology Briefs. J. P. Lynch, Richmond.—p. 79.
Roentgen Therapy of Certain Infections and Inflammations. C. W. Eley, Norfolk.—p. 80.
Recent Perils to Practice of Medicine as Viewed by a Rural Practitioner. J. P. Kent, Altavista.—p. 87.
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Use of Digitalis and Quinidine in Treatment of Heart Disease. W. C. Reed, Richmond.—p. 97.
Discussion of Renal Function Tests. J. F. Waddill, Norfolk.—p. 100.
*Nondiabetic Glycosuria: Report of Cases. S. C. Hall Jr., Danville.—p. 105.
Paresis and the Negro. L. Kolipinski, Petersburg.—p. 107.
Sulfapyridine in Treatment of Lobar Pneumonia: Report of Thirty-One Cases. C. F. James Jr., New York.—p. 109.
Schizophrenia Modified by Alcohol. L. I. Hallay, Fort Blackmore.—p. 111.
Agranulocytosis Following Use of Pyramidon and Neoprontosil: Case. J. H. Bailey and B. Katzen, Roanoke.—p. 112.
Occurrence of Multiple Cases of Infantile Paralysis in One Family. R. O. Jones, Burnsville, N. C.—p. 113.
Report of Stillbirth of Male Conjoined Twins, Gestation Eight and One Half Months, with Epigastric Attachment Extending from Third Rib to Umbilicus. H. C. Padgett, Roanoke.—p. 114.
Tularemia Treated by Sulfanilamide: Case. H. G. Hadley, Washington, D. C.—p. 115.

Nondiabetic Glycosuria.—Hall reports five cases of nondiabetic glycosuria. In spite of its prevalence the condition at times is not unrecognized, as the patients are subjected to a diabetic regimen. In some instances a long period of observation is necessary before the case can be put in a nondiabetic group. Some of these persons have been classified by Joslin as potentially diabetic. The diagnosis of diabetes mellitus may be made at least tentatively on a fasting venous blood sugar of 0.14 per cent or a value after a meal of 0.17 per cent. In nondiabetic cases the blood sugar should not exceed 0.17 per cent at its peak and should return approximately to the fasting level in two hours. Three of the patients whose histories the author presents received insulin with little if any effect for varying lengths of time, one for nearly nine years. None of the five patients gave a clinical history suggesting diabetes mellitus. With the exception of two, they did not complain of any symptoms; one of these two complained of weakness, lassitude and some weight loss, and the other of amenorrhea. Physical examination was essentially normal in all. Only one patient had a positive family history of diabetes mellitus. The pathologic physiology involved in benign glycosuria is not known. There are no signs or symptoms of renal inadequacy except the glycosuria. The blood sugar may be somewhat on the low side of normal. The patient who received insulin for nine years excreted variable amounts of sugar when taking it but, after taking dextrose for a sugar tolerance test, excreted no sugar at all. The benign course of the condition is well illustrated by this patient, who a year after discontinuing insulin looks and feels well.

Wisconsin Medical Journal, Madison

39: 77-152 (Feb.) 1940

Pulmonary Hypertension and Failure of Right Side of Heart. T. J. Dry, Rochester, Minn.—p. 89.
*Early Postoperative Feeding. P. H. Halperin, Madison.—p. 94.
Formation of Urinary Calculi Following Fracture: Case Report. C. A. Wood, Waukesha.—p. 97.
Bromism. O. C. Clark, Oconomowoc.—p. 100.
Improved Technic in Use of Kielland Forceps. J. B. Vedder, Marshfield.—p. 103.
Treatment of Atrophic Arthritis. A. C. Hansen, Milwaukee.—p. 106.

Early Postoperative Feeding.—Halperin employed early postoperative feeding in sixty-five unselected cases excluding, however, cases in which operations had been performed on the stomach or the biliary tract. The types of diets given were carbohydrate (cooked cereals, jello, custards, hard candy, toast and synthetic fruit juices), protein (gelatin, beef stock, soups, soft boiled eggs and lean meats), carbohydrate and protein and control diets (liquids for forty-eight hours and then a soft diet). Approximately 25 per cent of the twenty-three patients given the protein diet vomited almost immediately after its ingestion. This, the author believes, was psychic and due to the fact that the diet was not palatable. Most of the patients had to be forced to eat and many complained bitterly that they had no desire to eat such food. The average time postoperatively at which this diet was given was 10.8 hours. About half of these patients had mild gas pains before eating, and approximately 44 per cent experienced some form of transitory gas pain after eating. Flatus by rectum was observed twenty-seven hours postoperatively. Five of the group had spontaneous bowel movements, eliminating the necessity of routine enemas. Eleven patients were given a carbohydrate diet about nine hours postoperatively. Two had mild gas pains before eating and four had slight gas pains after eating. No patient in this group had distention. Routine enemas were given forty-eight hours postoperatively. One of these patients vomited after eating. The average postoperative time at which twenty patients were given the combined protein and carbohydrate diet was twelve hours. Nine of this group experienced gas pains prior to eating. Four had gas pains after taking the diet. None of the patients had distention. Flatus was noticed on an average of twenty-five hours postoperatively. Two had spontaneous bowel movements. Enemas were administered at approximately forty-eight hours postoperatively. The eleven patients given the control diet experienced, at some time or other during the forty-eight hours, gas pains varying in intensity. At the end of forty-eight hours they were placed on the usual soft diet. The average patient in this group began to pass flatus at the end of forty-five hours. There were no cases of distention. The author's conclusion is that early postoperative feeding is practical and obviously efficacious in combating postoperative gas pains and distention. Gas pains occur less often and peristalsis is reestablished earlier, as evidenced by the fact that patients begin to pass flatus sooner. The type of diet administered is important. It should be of semisolid consistency and should not contain foods that might produce reflex nausea. Fats should be excluded in the early postoperative diet, since they tend to slow up peristalsis and inhibit to some degree the digestion of carbohydrates. With the exception of orange juice and milk, carbohydrate foods such as toast, cooked cereals, gruels, hard boiled eggs, gelatins, custards and mashed potatoes make up an ideal postoperative diet.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Heart Journal, London

2: 1-62 (Jan.) 1940

*Electrocardiographic Findings in Anemia. P. Szekely.—p. 1.
U, the Sixth Wave of the Electrocardiogram. C. Papp.—p. 9.
Psychologic Treatment of Cases with Cardiac Pain. G. Bourne and E. Witthower.—p. 25.
Analysis of Fifty Normal Electrocardiograms Including Lead IV. J. Hoskin and P. Jonescu.—p. 33.
Electrical Axis Deviation of Fifty Normal Electrocardiograms. J. Hoskin and P. Jonescu.—p. 47.
Relative Value of Certain Digitalis Preparations in Heart Failure with Auricular Fibrillation. W. Evans.—p. 51.

Electrocardiographic Changes in Anemia.—Szekely found with the aid of electrocardiograms abnormalities in twenty-three of seventy-six cases of anemia with no clinical evidence of cardiovascular disease. Most frequently flattening of the T wave occurred, less frequently depression of the ST segment and low voltage. In a case of hypochromic anemia inversion of the T wave in leads 2 and 3 occurred after a profuse hematemesis. These electrocardiographic changes disappeared shortly after the anemia was improved slightly. Experimental observations can be applied only with reserve in the clinical field. Nevertheless a correlation between anemia and cardiac disturbances resulting from anoxemia of the heart muscle suggests itself, especially the occasional disappearance of both clinical and electrocardiographic abnormalities after improvement of the anemia. In the author's cases there was no close parallelism between the degree of anemia and the cardiac disturbances. It seems probable that, both in acute and in chronic anemia, angina pectoris or electrocardiographic changes are not due merely to the anemia causing anoxemia of the heart muscle but also to some other factor. In acute posthemorrhagic anemia this additional factor seems to be of reflex vasomotor character. In such instances the coronary volume flow may not be adapted to the acutely altered circulation, and acute coronary insufficiency may result with clinical or electrocardiographic manifestations. The case of hypochromic hemorrhagic anemia could be explained in this way. In chronic anemia the primary myocardial anoxemia, as the direct result of the diminution of the oxygen-carrying power of the blood, may have a more decisive role. Toxic factors must also be taken into consideration, as they may affect the myocardium directly. Such might have been the case in the chronic cases with low voltage in which the electrocardiographic abnormalities were irreversible in spite of temporary improvement of the anemia.

British Journal of Dermatology and Syphilis, London

52: 43-72 (Feb.) 1940

Dermatology and Folklore. J. D. Rolleston.—p. 43.
Median Mental Sinus. G. Duckworth.—p. 57.
Schamberg's Disease. W. J. O'Donovan.—p. 60.

British Journal of Ophthalmology, London

24: 1-52 (Jan.) 1940

Response of Eye to Light in Relation to Measurement of Subjective Brightness and Contrast. W. D. Wright.—p. 1.
Mechanism of Dark Adaptation: Critical Résumé. R. J. Lythgoe.—p. 21.
Sclerocylindric Contact Lenses: Preliminary Note. F. A. Willimason-Noble, J. Dallos and Ida Mann.—p. 43.

24: 53-104 (Feb.) 1940

Improvised Eye Irrigator for Use in the Field. H. B. Stallard.—p. 53.
Origin of Abnormal Retinal Correspondence. T. a'B. Travers.—p. 58.
Buphthalmos with Facial Nevus and Allied Conditions. A. J. Ballantyne.—p. 65.
Study of Effects of Liquid Mustard Gas on Eyes of Rabbits and of Certain Methods of Treatment. P. C. Livingston and H. M. Walker.—p. 67.

British Journal of Radiology, London

13: 1-36 (Jan.) 1940

New Technic of Treatment of Carcinoma of Cervix Uteri by Combining X-Rays and Radium. J. Z. Walker.—p. 1.
Physical Investigation of Contribution of Photo-Electrons from Sulfur to X-Ray Ionization. L. H. Gray.—p. 25.
Relative Response of Skin of Mice to X-Radiation and Gamma Radiation. J. C. Mottram and L. H. Gray.—p. 31.
Nonrotation of Colon. H. G. Hadley.—p. 35.

13: 37-72 (Feb.) 1940

Recent Advances in Roentgen Diagnosis of Gastric Cancer. R. Ledoux-Lebard.—p. 37.
Intussusception: Radiologic Study. E. R. Williams.—p. 51.

British Medical Journal, London

1: 201-242 (Feb. 10) 1940

Interaction In Vitro of Fibroblasts and Sarcoma Cells with Leukocytes and Macrophages. R. J. Ludford.—p. 201.
Effect of Estradiol Benzoate on Amount of Gonadotropin Found in Pituitary Gland and Urine of Postmenopausal Women. I. W. Rowlands and E. P. Sharpey-Schafer.—p. 205.
Convergence Deficiency: Condition, Its Occurrence in Private Practice and Results of Treatment. Ida Mann.—p. 208.
Results of Ambulant Treatment of Peptic Ulcers. D. Ferriman.—p. 210.
*Agranulocytosis Following Sulfapyridine Therapy. B. Pringle, G. C. Dockeray and R. H. Mitchell.—p. 212.

Granulocytopenia Following Sulfapyridine Therapy.—Pringle and his co-workers report a case of granulocytopenia occurring during sulfapyridine therapy for pneumonia. No other drug known to cause granulocytopenia was administered to this patient. The recovery of the patient was rapid and uninterrupted following transfusion, despite the fact that the diagnosis was not made until there were no granular cells in the blood. "Angina," with the exception of slight ulcerative changes in the mouth, was absent. The only symptom was persistent severe pain in the legs. Evidence of any other toxic reaction to the drug was absent. The authors review similar previously reported cases.

Edinburgh Medical Journal

47: 81-152 (Feb.) 1940

Nicotinic Acid Treatment of Pellagra: Report of Case Occurring in Edinburgh. D. S. Robertson.—p. 81.
Tuberculous Pyopneumothorax, with Special Reference to Certain Points in Its Management. R. Y. Keers.—p. 86.
Occupational Therapy. J. Cunningham.—p. 96.
The Problem of the Virulence of Tubercle Bacillus. W. T. Munro.—p. 110.
Dynamics of Crowd Infection. A. G. McKendrick.—p. 117.

Journal of Endocrinology, London

1: 231-366 (Nov.) 1939

Observations Related to Swelling of Sexual Skin in Rhesus Monkeys. A. G. Ogston, J. St. L. Philpot and S. Zuckerman.—p. 231.
Species Variation in Thyrotropic, Gonadotropic and Prolactin Activities of Anterior Hypophysial Tissue. M. R. A. Chance, I. W. Rowlands and F. G. Young.—p. 239.
Effects of Estrogen and Androgen Injections on Reproductive Organs in Male Rats and Mice. R. Harsh, M. D. Overholser and L. J. Wells.—p. 261.
Inadequacy of Vaginal Smear in Rat as Index of Ovarian Dysfunction Caused by Diet. S. C. Freed, O. Hechter and S. Soskin.—p. 268.
Studies on Relationship of Vitamin E (Tocopherols) to Endocrine System. J. C. Drummond, R. L. Noble and Margaret D. Wright.—p. 275.
Effect of Subcutaneous Implantation of Adrenalin Tablets on Blood Sugar and Milk Composition in Lactating Ruminants. A. C. Bottomley, S. J. Folley, F. H. A. Walker and H. M. S. Watson.—p. 287.
Uterus Masculinus of Rabbit and Its Reactions to Androgens and Estrogens. Ruth Deanesly.—p. 300.
Modification of Effectiveness of Gonadotropic Extracts. Ruth Deanesly.—p. 307.
*Effect of Route of Administration on Multiple Activities of Testosterone and Methyl Testosterone in Different Species. C. W. Emmens and A. S. Parkes.—p. 323.
Some Biologic Properties of Anhydro-Hydroxy-Progesterone (Ethinyl Testosterone). C. W. Emmens and A. S. Parkes.—p. 332.
Anterior Pituitary Fractions and Carbohydrate Metabolism: I. Preparation and Properties of Diabetogenic Extracts. F. G. Young.—p. 339.
Urinary Gonadotropic Extracts and Anaphylaxis in Vitro. M. van den Ende.—p. 356.

Activity of Androgens and Route of Administration.—Emmens and Parkes studied the effectiveness of testosterone and methyl testosterone in capons, rats and rabbits when administered by inunction, orally and parenterally. Testosterone is much less active by mouth than by injection in tests for androgenic activity in the capon and castrated male rat, in metrotropic tests on spayed rats or immature rabbits, and in tests for progesterone-like activity in rabbits. Methyl testosterone, however, is almost as active by mouth as by injection in causing progestational proliferation in rabbits, and it has a relatively greater activity by mouth in the other tests than has testosterone. When given orally instead of by injection to rats, its androgenic activity decreases much less than its power of causing an increase in uterine weight. Methyl testosterone is more potent than testosterone as an androgen in rats, but less potent in capons, and more potent than testosterone in the progestational tests by either route of administration. The two substances are about equally active in causing uterine growth in spayed rats and immature rabbits.

Journal of Neurology and Psychiatry, London

3: 1-100 (Jan.) 1940

*Emotional and Somatic Response of Schizophrenic Patients and Normal Controls to Adrenalin and Doryl. J. B. Dynes and H. Tod.—p. 1.
Distribution of Commissural Fibers in Corpus Callosum in Macaque Monkey. S. Sunderland.—p. 9.
Behavior and Mood Cycles Apparently Related to Parathyroid Deficiency. C. P. Richter, W. M. Honeyman and H. Hunter.—p. 19.
Hypoglycemic Shock and Grasp Reflex: Effect of Insulin Shock on Bulbocapnine Catalepsy in Monkeys. A. Kennedy.—p. 27.
Degeneration of Papillomacular Bundle in Apes and Its Significance in Human Neuropathology. H. J. Scherer.—p. 37.

Response of Schizophrenic Patients to Drugs.—Dynes and Tod compared the emotional and somatic reactions of ten schizophrenic patients and six normal control subjects after intramuscular injection of epinephrine and carbaminoylcholine chloride. There was no significant difference in the somatic responses of the two groups of subjects, although the schizophrenic group exhibited more variability of response to both epinephrine and carbaminoylcholine chloride, tending to bear out the observations of others to the effect that the adaptive mechanisms of the schizophrenic patient to preserve the "steady state" are defective under conditions of stress. Carbaminoylcholine chloride injected intramuscularly produced an excellent peripheral autonomic response in both the schizophrenic and the normal subjects, but no emotional disturbance (anxiety or fear) in either. The clearcut and definite failure of epinephrine to arouse the anxiety or fear response in the schizophrenic patient as compared with the normal control subject is significant and points to a disordered emotional mechanism at a physiologic level. Experimental data are presented which only indirectly localize this break in the chain of physiologic response. The results suggest possibilities for investigation in an effort to understand better the central emotional mechanism.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

46: 941-1080 (Dec.) 1939

Antepartum Hemorrhage. N. Pasha Mahfouz and I. Magdi.—p. 941.
*Ovarian Dysmenorrhea: Its Etiology, Diagnosis and Treatment. O. Browne.—p. 962.
Estrogens and Carcinoma of Uterus. A. A. Gemmell and T. N. A. Jeffcoate.—p. 985.
Adenocarcinoma of Uterus Subsequent to Simple Intra-Uterine Polyposis. R. E. Hirson.—p. 994.
Value of Cephalometry in Estimation of Fetal Weight, Based on Measurements of 1,010 Infants. J. G. H. Ince.—p. 1003.
Labor Obstructed by Dermoid Cyst of Rectovaginal Septum. G. Maizels.—p. 1011.
Bilateral Cystine Renal Calculi and Pregnancy. J. Young and J. Carver.—p. 1015.
Unusual Case of Adenocarcinoma of Body of Uterus. A. E. Chisholm and R. L. Ferguson.—p. 1019.
The Simpson Memorial Maternity Pavilion, Royal Infirmary, Edinburgh. R. W. Johnstone.—p. 1020.

Ovarian Dysmenorrhea.—Ovarian dysmenorrhea, according to Browne, is a definite clinical entity with characteristic symptoms and signs which allow of an accurate diagnosis. It is present alone in about 11.9 per cent of all cases of dysmenorrhea but may be associated with dysmenorrhea of uterine origin, thus constituting "mixed" dysmenorrhea. True ovarian dysmenorrhea can be completely cured by bilateral ovarian denervation. The author did not observe any ill effects following this operation. In the severe and intractable dysmenorrhea of uterine and ovarian origin both bilateral ovarian denervation and presacral sympathectomy are probably indicated. In an effort to separate clinically uterine from ovarian dysmenorrhea the author devised a sound test. The passing of a sterile uterine sound, heretofore regarded as a difficult procedure in such cases owing to the likelihood of the internal os being tight, proved to be simple and was not followed by any known immediate or remote ill effects. Pregnancy, cervical infection or other contraindications should be excluded before the sound is passed. In several cases a small intra-uterine bag inflated to 5 cc. capacity was used, with full aseptic precautions, to test for uterine pain. In others, when the fallopian tubes of the patient were blocked, Rubin's apparatus was used up to 300 mm. of mercury pressure. From these methods the author concluded that typical uterine pain is accurately referred to the midline of the lower part of the abdomen in the immediate suprapubic area, although it may sometimes reach as high as the umbilicus. This was true in 49 per cent of the patients examined. In 11 per cent of somewhat exceptional instances of uterine dysmenorrhea the passing of a uterine sound produced atypical referred pain in some other part of the lower abdominal area. In most of these there was some palpable pelvic abnormality. The passing of the sound was painless in approximately 36 per cent of the patients, many of whom were not suffering from dysmenorrhea; it produced pain referred exactly to the umbilicus in 2 per cent, and to the midline of the vulva about the position of the clitoris in the other 2 per cent. Pathways for painful ovarian stimuli exist in the ovarian nerves. The neurogenic etiologic theory of ovarian dysmenorrhea is accepted by the author as the most likely and his microscopic material confirms the observations already published on this matter. Sclerocystic ovarian changes are constant in severe ovarian dysmenorrhea and are probably secondary to preexisting ovarian nerve lesions. Cervical dilation, with or without uterine curettage, relieves only those cases of uterine dysmenorrhea in which there is no serious premenstrual discomfort or pain. It is pointed out that Cotte's 60 per cent cure rate of uterine dysmenorrhea by presacral sympathectomy, when considered along with the author's 11 per cent rate in cases of isolated ovarian dysmenorrhea following bilateral ovarian denervation, suggests that the remaining 25 to 30 per cent of cases of severe dysmenorrhea are of the "mixed" type or, possibly, of endocrine origin.

Lancet, London

1: 255-302 (Feb. 10) 1940

Rickettsia Diseases of Malaya: Identity of Tsutsugamushi and Rural Typhus. R. Lewthwaite and S. R. Savoor.—p. 255.
Recurrent Traumatic Herpes. G. M. Findlay and F. O. MacCallum.—p. 259.
Dosage of Sulfanilamide Derivatives for Children. M. Hynes.—p. 261.
*Tuberculosis in Medical Students: Diagnostic Service at University College Hospital Medical School. P. D. Hart, Gwen Hilton and A. Morland.—p. 263.
Hemiplegia Complicating Sodium Diphenyl Hydantoinate Therapy of Epilepsy. D. Blair.—p. 269.

Tuberculosis in Medical Students.—Hart and his associates state that about a third of the total deaths from disease among young adults are due to pulmonary tuberculosis and that this age group shared least in the general decline in mortality from tuberculosis in the present century. The committee of University College Hospital medical school introduced a scheme for a periodic medical examination of students occupied in clinical training or in junior qualified appointments at the hospital in order to reduce the morbidity from pulmonary tuberculosis by early detection. The system has now been in operation for more than three years. The program consists of periodic radiography combined with history taking and latterly with Mantoux testing. The average population at risk has been about 250, with a gradually changing makeup. Between February 1936 and June 1939 the number showing lesions of some importance amounted to twenty-six of a total of 417 students examined, an incidence of 6.2 per cent. In seventeen of the twenty-six the lesions were believed to have had their onset during the clinical course and in the remaining nine to have originated previously. Pulmonary fluffy shadows were observed in thirteen, pulmonary "coin" shadows, considered to represent early primary foci, in four, pleurisy in five, gross healed pulmonary lesions in two and extrapulmonary tuberculosis in two. Eight were advised sanatorium or hospital treatment, four were advised restricted life without cessation of work and fourteen were recommended to pursue normal lives under closer observation. Of the eight sanatorium cases, five presented fluffy pulmonary shadows, one had a pleurisy with effusion and two were cases of extrapulmonary tuberculosis. All but one of the eight exhibiting fluffy pulmonary shadows accepted the advice. Of the five students with fluffy pulmonary shadows advised sanatorium treatment, two exhibited cavitation (one with positive sputum), one had a fibrocaseous lesion with positive sputum, one had had a spontaneous pneumothorax previously and one showed a persistently raised sedimentation rate. In all these cases, however, the symptoms referable to the chest at a time when the fluffy shadows were first discovered were minimal, and in four the lesion was recognized in the course of a systematic routine examination, only one because of subjective complaints. The type, localization and course of the fluffy shadows varied. The progress of the students with such shadows on sanatorium treatment (four of the five so advised) has been satisfactory. The lesions were of a limited extent, and those with cavitation reacted well to pneumothorax therapy.

All these students returned to work and have since qualified. The progress of the students advised restricted or normal life without cessation of work has so far been satisfactory. The response to the present voluntary program among the students eligible for enrolment has been more than 98 per cent, and the results have fully justified the expense and the effort involved.

Medical Journal of Australia, Sydney

1: 107-142 (Jan. 27) 1940

Medical Men and Books. K. Inglis.—p. 107.
Use of Sulfanilamides in Bacterial Infections. G. A. Penington.—p. 113.
*Concentration of Sulfanilamide in Saliva Following Oral Administration. S. Williams, Beryl Splatt and Rachel Jakobowicz.—p. 120.

Sulfanilamide in Saliva.—In spite of the value of sulfanilamide in most infections caused by hemolytic streptococci in man, it appears to be valueless in the treatment of scarlet fever in the early stage of toxemia. If the drug when administered by mouth is capable of inhibiting multiplication of hemolytic streptococci in the throat it should have a decisive prophylactic effect in scarlet fever. Williams and his associates cite studies which show that the problem of sulfanilamide excretion in the saliva of man is not simple. Excretion occurs only in the saliva at levels of blood sulfanilamide which vary greatly from subject to subject. Thus though a dose of 6 Gm. (70 or more mg. per kilogram of body weight) of sulfanilamide with large amounts of water given by a Rehfuss tube appears to ensure excretion of a reasonable amount of sulfanilamide in the saliva, a dose of 4 Gm. (50 mg. per kilogram of body weight) was not adequate to cause such a secretion. It is unlikely therefore that the saliva contained sulfanilamide in concentrations sufficient to be effective. Sulfanilamide causes neither stimulation nor inhibition of the salivary glands as judged by the volume of saliva excreted and the concentration of urea in it.

Tubercle, London

21: 81-120 (Dec.) 1939

*Thoracoscopy and Adhesion Section, with Special Reference to Indications and Results. J. Smart.—p. 81.
Tuberculosis in Burma. S. L. Cummins.—p. 97.

Thoracoscopy and Adhesion Section.—Smart believes that thoracoscopy and section of adhesions, by converting an imperfect artificial pneumothorax into a complete one, is a measure that has an important place in the complementary treatment of pulmonary tuberculosis. Of fifty-two consecutive thoracoscopies followed up for two years, the adhesions were divided in ten cases to produce a more perfect artificial pneumothorax; in twenty-seven the adhesions were divided because the artificial pneumothorax was unsatisfactory. Five patients were extremely ill and the adhesions were divided as a last resort. It was impossible to free the lung in one session in eight of ten patients, and two thoracoscopies were performed on each of them. In two patients a bilateral artificial pneumothorax was present at the time of the operation; in one there was no undue dyspnea but in the other the dyspnea was such that it was impossible to do more than look at the adhesion and withdraw the instrument at once. The mechanical results in the first ten cases were free artificial pneumothorax in seven and improved collapse in three. At present eight of these patients are in good health with no tubercle bacilli present and the health of two is improved. Of the twenty-seven patients, fourteen obtained a free artificial pneumothorax, eleven an improved collapse and the collapse of two remained the same. Seventeen of these twenty-seven patients are in good health with no tubercle bacilli, four are in fair health, three are in relapse or the condition has extended to the other side and three are dead. Of the five patients of the last group, four obtained an improved collapse and in one the collapse remained the same; two are in good health, one in fair health and two are dead. Empyema occurred in six instances of the fifty-two operations. The author believes that thoracoscopy is indicated for all patients who have adhesions and should not be confined only to those in whom an artificial pneumothorax is unsatisfactory. At the same time, when the artificial pneumothorax is satisfactory the adhesion should be cut only if the operator is certain that there is no risk of damage to the lung or the great vessels. The final results of artificial pneumothorax treatment have been considerably improved as a result of thoracoscopy.

Chinese Medical Journal, Peiping

58: 403-500 (Nov.) 1939

*Anemia from Blood Donation: Hematologic and Clinical Study of 101 Professional Donors. I. Snapper, S. H. Liu, H. L. Chung and T. F. Yu.—p. 403.
Hepatitis Following Sulfanilamide Therapy: Case Report. W. N. Bien and C. L. Tung.—p. 424.
Syphilis of Lung: Report of Three Cases Observed in North China. C. K. Hu, C. N. Frazier and C. K. Hsieh.—p. 431.
*Isolation of Treponema Pallidum from Blood During Primary Incubation Period of Human Syphilis. C. N. Frazier and H. C. Pian.—p. 441.
Dentigerous (Follicular) Cyst: Study of Fifty-Four Cases. A. F. Buranoff, C. S. Chang and H. T. Kimm.—p. 446.
Studies on Types of Corynebacterium Diphtheriae in Shanghai. H. Yü and Y. F. Hu.—p. 456.
Further Investigations on Schistosomiasis Japonica in Futsing, Fukien Province. C. C. Tang.—p. 462.
Trachoma in Chengtu, Szechwen: Review of 468 Cases. W. S. Mao.—p. 474.

Anemia of Blood Donors.—The studies of Snapper and his associates refute the general impression that recurrent donations of blood produce no harmful effects on the donors. Of 101 professional blood donors who had donated from 0.85 to 25 liters of blood in the course of from two months to ten years, seventy-six donors were found with a hemoglobin below 12 Gm., forty-four below 10 Gm., sixteen below 8 Gm. and three below 6 Gm. It was found that the frequency and the extent of the anemia increased with the total amount of blood withdrawn or the duration of service. Poor diet was considered to be a most important factor in the sluggish hemopoietic activity. Twenty of the ninety-three donors examined at the outpatient medical clinic were undernourished, twenty-nine had extreme pallor, glossitis was observed in twenty-five, systolic murmurs at the apex were heard in thirty-three, a palpable or an enlarged spleen was evident in twenty and the liver was either palpable or enlarged in eight. Six of the anemia donors were studied while resident in the hospital. The anemia proved to be of the microcytic hypochromic type, which is usually seen in cases in which there is chronic loss of blood. Glossitis, splenomegaly and achlorhydria were present in most of these cases. Treatment with large doses of iron resulted in prompt improvement, while cessation of blood donation was uncertain and less effective in bringing about a remission. Leukopenia, lymphocytosis and eosinophilia were common and often very marked. These usually disappeared on discontinuance of blood donation whether additional iron therapy was or was not given.

Spirochaeta Pallida in Blood During Primary Syphilis.—Frazier and Pian report the isolation of Spirochaeta pallida in the blood during the primary stage of syphilis. The case is that of a Chinese blood donor who had received frequent physical and serologic examinations during the course of his service. In September and November 1938 no evidence of syphilis was found on physical examination and serologic tests gave negative results. Between Nov. 7 and Dec. 15, 1938, he had four venereal exposures with three women. On Dec. 22, 1938, he gave 150 cc. of his blood for transfusion. At that time there was no penile sore or other syphilitic lesion and the Kline reaction was negative. On Jan. 6, 1939, he was again examined and found to be normal. The Kline reaction was again negative. On January 11 an ulcer of the prepuce was first noticed. This was twenty days after the transfusion. On January 26 he reported to the syphilis clinic with a typical chancre of the prepuce. Darkfield examination showed the presence of many spirochetes. The blood serum Wassermann reaction was anticomplementary but the Kahn and Kline reactions were positive. The recipient, a Chinese boy 8 years of age, had no evidence of syphilis, either acquired or congenital, before the transfusion of blood on Dec. 22, 1938. On Jan. 28, 1939, thirty-seven days after transfusion, he first noticed pain in both legs and a tender swelling on each anterior tibial surface. This was followed by pain and swelling of both forearms, fever and general malaise. On March 2 the recipient had a generalized macular eruption and a fulminating type of osteomyelitis and periostitis of both frontal and parietal bones, and of all the long bones except the femurs. The blood Wassermann reaction was strongly positive. On March 10, seventy-eight days after the transfusion, 1 cc. of his blood was inoculated into each testis of two normal rabbits. An acute orchitis developed in one of these animals seventy days after inoculation, and Spirochaeta pallida was identified in the aspirated testicular fluid by darkfield examination. The other animal showed no clinical or serologic evidence of infection during a period of twelve weeks.

Archives Méd.-Chir. de l'App. Respiratoire, Paris

14:1-80 (No. 1) 1939

Study of Pulmonary Lobules and of Their Air-Conducting Canals. V. E. de Pablo.—p. 1.
Roentgenkymography in Study of Respiratory Kinematics. A. Rodrigues and R. Carvalho.—p. 24.
*Thoracoplasties and Mediastinal Flutter: Study on Mobility of Mediastinum. A. Bernou, H. Fruchaud and L. Marcenaux.—p. 34.
Section of Adhesions: Pneumococcic Purulent Pleurisy Treated by Sulfanilamides; Pulmonary Miliary Tuberculosis with Bacillemia. D. Douady, J. Braillon and Geneviève Georges.—p. 46.
*Pulmonary Forms of Besnier-Boeck-Schaumann's Disease. G. Thoyer.—p. 55.

Thoracoplasties and Mediastinal Flutter.—According to Bernou and his collaborators, mediastinal flutter began to receive attention with the introduction of paravertebral costal resections to include nearly all of a hemithorax. Accurate descriptions of this complication were first given by Sauerbruch and by César Roux. It may develop in the course of, or immediately after, a total thoracoplasty, when with each inspiration the healthy lung draws the mediastinum toward itself, the latter being no longer held back by the elasticity of the opposite lung. Thus the inspiratory effort becomes ineffectual. Rehn demonstrated the important role of the anterior mediastinum (retrosternal mediastinal space) in maintaining the equilibrium of the cardiovascular and respiratory functions. The authors discuss the roentgenologic technic of Rehn in investigation of the mobility of the anterior mediastinum and his method of fixation of the mediastinum. It is possible occasionally to observe on the screen considerable movements of the mediastinum in pneumothorax. The authors feel that an anterolateral thoracoplasty should never be attempted in the presence of a mobile mediastinum, which during examination in the lateral decubitus shows a deviation of more than 2 cm. (especially if the deviation attains from 4 to 6 cm.). It is less dangerous in such cases to perform a paravertebral or a subscapular thoracoplasty. In the presence of a flexible mediastinum, a superior paravertebral thoracoplasty as a primary intervention does not prevent mediastinal flutter in the later operations. The patient thus will be all the more exposed, because the wall will at a given moment remain flexible on a more extensive surface, notably in front, and it is evident that the mobility of the mediastinum will be more pronounced than before the operation. To avoid this complication they recommend that (1) the number and extension of costal resections in the first stage of the operation be reduced (it is better to expose the patient to a supplementary intervention than to mediastinal flutter) and (2) that operations be spaced so that some resistance of the wall has time to develop. Extraperiosteal costal resections and the application of formaldehyde to the periosteal beds should be avoided in these cases, because they risk leaving the walls flexible for too long a period. In the method employed by the authors the first rib is not resected until the second operation. This is postponed for three or even four weeks so as to obtain a certain resistance of the wall.

Pulmonary Forms of Besnier-Boeck-Schaumann's Disease.—The first case of cutaneous infiltration, according to Thoyer, was described by Besnier in 1889 under the term lupus pernio. Ten years later Boeck saw the nodular form of the same infiltration and designated the lesion as a sarcoid, and somewhat later, recognizing their lupiform course, he designated them as lupoids. Heerfordt in 1909 described a syndrome which comprised ocular lesions, swelling of the parotids and bilateral facial paralysis. No relationship was suspected between this uveoparotiditis and the cutaneous lesions until Pautrier recognized their common origin. At present, the Besnier-Boeck disease is recognized as a general disorder capable of multiple localizations, the cutaneous and ocular forms of which are the most striking. The concept of a systemic character is based on the clinical and histologic studies of Schaumann, who in 1914 proved the identity of the diffuse infiltrations of Besnier and the sarcoid of Boeck, finding at the same time identical tuberculoid infiltrations in the lymph nodes, the tonsils, the bones and the lungs. Thoyer devotes particular attention to the pulmonary form, which may be readily mistaken for fibrous tuberculosis. Some investigators insist that the pulmonary form of Besnier-Boeck-Schaumann's disease is especially frequent. The process is nearly always torpid. It does not give rise to notable functional or auscultatory signs and is usually discovered by x-ray examination. Three types of roentgenograms are recognized: 1. The most frequent and the most characteristic consists of a micronodular infiltration, the nodules resembling those of miliary tuberculosis. 2. The infiltration takes on the form of strands, or is marmoreal, resembling that of fibrous tuberculosis. 3. Cloudiness of the perihilar region suggests a selective lymphatic involvement which may be mistaken for mediastinal adenopathy of Hodgkin's disease. There may be a combination of lesions and a diversity of forms. Recently several authors have emphasized the existence of a type in which the pulmonary lesions predominate and are often associated with a superficial lymphatic involvement, a lymphopulmonary form of the disease. From the pathologic point of view, Besnier-Boeck-Schaumann's disease differs from tuberculosis by the absence of caseous degeneration. It is assumed that a specific, as yet unidentified, virus is the cause of the disease.

Journal de Chirurgie, Paris

55:97-192 (Feb.) 1940

Fractures of Tibial Plateau. M. van der Ghinst.—p. 97.
*Extensive Intervention in Cancer of Thyroid. M. Dargent and M. Bérard.—p. 131.

Intervention in Cancer of Thyroid.—Dargent and Bérard studied 100 cases of cancer of the thyroid at the Cancer Hospital in Lyons. Two main types of thyroid cancer are differentiated. The anatomic characteristics of one resemble those of the fetal or the adult thyroid. These are trabecular, vesicular and trabeculovesicular cancers, papillary cancer and other rare forms. In the second, the morphologic appearances differ from those of the thyroid. These are the Herrenschmidt cancer, sarcoma, reticulosarcoma, plasmocytoma and fibroma. In addition to these two types there exist numerous atypical epitheliomas. All the cancers of the first type are of a limited malignancy, while those of the second type are extremely grave. In atypical epitheliomas the survival generally does not exceed three years. The trabeculovesicular cancers, the most common type of the first group, can be extensively removed even when accompanied by metastases, and a survival of more than ten years may be obtained. The metastases may give the impression of original tumors as in benign, so-called metastatic goiter. Surgical records and the examination of the specimens revealed the presence of invaded lymph nodes along the carotid chain and the veins of the neck and early neoplastic proliferations in the lumen of the thyroid vein, a short time after the intracapsular degeneration of the thyroid adenoma preexisting nearly always in these forms. With regard to roentgenologic sterilization of the operative field as opposed to the extensive operation, it may be said that, while it is effective in the treatment of metastases, its effect on the cancerous islands left behind is illusory. The authors review types of extensive interventions proposed by L. Bérard and Dunet, Joll and the Criles. They describe an extensive intervention in which extirpation *en bloc* of the sternocleidomastoid, the superficial aponeurosis, the omohyoid, the subhyoids, the median aponeurosis, the internal jugular vein, the superior thyroid and the entire tumor is done after the dissection of the recurrent nerve and the ligation of the arterial pedicles as far as possible. This operation must be considered as a systematic removal of cancer of the thyroid at the onset or in the course of its development. It is not applicable in extensive or relapsing cancers. It must be performed even when there are no signs of invasion of the lymph nodes. It is indicated in two types of cases: (1) the classic cases of unusual increase in volume of a benign tumor of the thyroid, (2) cases in which biopsy discloses early malignancy after a subtotal resection of a goiter. The contraindications are (1) impairment of the general state with extreme cachexia and considerable dissemination of metastases, (2) adherence to the trachea and the esophagus, confirmed by endoscopy, (3) previous knowledge of the character of the tumor. In case of tumors of the connective tissue these extensive operations are not justified. It is not necessarily contraindicated in the presence of paralysis of the recurrent nerve, for the latter does not always indicate invasion of the larynx, or in the presence of osseous metastases which are sensitive to roentgen therapy. The roentgen therapy of the skeleton must be made at least fifteen days after the operation, before roentgen therapy on the operative wound.

Presse Médicale, Paris

48: 97-120 (Jan. 31-Feb. 3) 1940

*Curable and Atypical Forms of Postanginal Septicopyemia Due to Bacillus Funduliformis. A. Lemierre, A. P. Guimaraes and J. Lemierre.—p. 97.
Nerve Lesions: Results of Surgical Treatment and Operative Indications. R. Dumas.—p. 99.
Spinal Injections of Sulfanilamide in Treatment of Purulent Meningitis. R. Martin, Panthier, Nonaille and Mlle. Hamond.—p. 101.

Atypical Forms of Postanginal Septicopyemia.—Lemierre and his collaborators report ten cases of atypical postanginal septicopyemia due to Bacillus funduliformis, in all of which a cure was effected. The age level of the patients was between 19 and 31 years. Medication employed in several cases and referred to as 1162 F was administered daily in doses of 4 Gm. after the first diagnostic suspicion, though the authors make no claims for its specificity. The atypical features included the following elements. Hemoculture did not always show bacterial presence initially. In two cases the bacillus was recovered only in the pus of natal abscesses; in another its presence could be established only indirectly by a flocculation test. Several cases presented a pyrexia-apyrexia fluctuation with the general health unimpaired between the febrile attacks. Several cases did not show typical arthritis. In several a submaxillary involvement was noted that was painful on palpation. The time of recovery varied considerably. One patient recovered within the period of two weeks. One presented a complete absence of pulmonary signs and articular pains. Pleural effusion was occasionally observed, sometimes only in sterile form. The cases cited demonstrate that clinical evidence increasingly shows that fatal prognosis does not apply always to postanginal septicopyemia. Whether these cases represent a special benignancy due to local conditions is a possibility. Some of the atypical cases present a grave appearance but go on to recovery contrary to expectations. Others possess the three characteristic symptoms (pyrexia preceded by intense chills, pulmonary infarcts, arthritis) and have a short evolution. Others are characterized by high fever but show no sequels; others again, after a brief and variable period of septicemia, show pulmonary, pleural or articular metastatic lesions. The single case that was almost afebrile could be determined only indirectly by the Laporte-Brocard flocculation test.

Annales Pædiatrici, Basel

154: 121-248 (Dec.-Jan.) 1939-1940

Observations on Postvaccinal Encephalomyelitis in the Netherlands During Last Few Years. B. Brouwer.—p. 121.
*Familial Infantile Form of Diffuse Cerebral Sclerosis (Krabbe). Cornelia de Lange.—p. 140.
Diagnosis of Pulmonary Agenesia. O. Saxl.—p. 180.
*Paralytic Manifestations After Synthetic Antimalarial Medicaments. K. Choremis and G. Spiliopoulos.—p. 194.
Etiology of Besnier-Boeck's Disease. P. Spiro.—p. 199.
Recurrent Ileus. S. Wolff.—p. 211.

Familial Infantile Form of Diffuse Cerebral Sclerosis.—Scarcity of reports on the familial infantile form of diffuse cerebral sclerosis, first described by Krabbe, suggests that such cases are rare. Lange believes that a better knowledge of the symptomatology, with its many characteristic aspects, might lead to the recognition of a greater number of cases of this disorder. She reports the histories of four children in one family who successively manifested the same cerebral syndrome of general rigidity, opisthotonos and deterioration of the intelligence. The first child, a girl, died at eight months; then there were twins (girls), one of whom died at thirteen and one half months. The author was able to examine the brain of this child. The brain presented some congenital abnormalities. Moreover, there was a diffuse demyelinization of the entire cerebrum and of the parts of the spinal cord available for examination. There also existed extensive proliferation of normal and of pathologic neuroglia. The degree of fibrosis differed in various parts of the nervous system. The nerve cells were more or less intact. Some aspects point to a primary disease of the neuroglia. The author reviews cases from the literature and compares them with the familial juvenile form (Scholz) and with other leukodystrophies. More cases will probably be discovered if the following characteristic symptoms are kept in mind: familial occurrence, onset of illness usually a few months after birth, increasing general stiffness, often crossing of the legs (scissors position), opisthotonos, manifestations simulating spasmophilia and deterioration of the intelligence. The intracranial pressure is not increased.

Paralytic Manifestations After Antimalarial Medicaments.—Choremis and Spiliopoulos report two cases in which excessive doses of antimalarial drugs produced paralysis which chiefly affected the respiratory muscles. The first patient was a child aged 3. For three days the child had been given daily 0.01 Gm. of plasmochin, a synthetic preparation of quinoline, 8-(-diethylamino-isopentyl-) amino-6-methoxychinolin. On the fourth day the child swallowed accidentally four tablets of 0.01 Gm. each. On the following day there were cyanosis, dyspnea, hoarseness, difficulty in swallowing and general weakness with paresis of the legs. Irregular respiratory rhythm of the Cheyne-Stokes type developed, probably as the result of an impairment of the respiratory center. It was observed that during attacks of fever the respiration became normal, but during the nonfebrile intervals the child had attacks of Cheyne-Stokes respiration. The second patient, a boy aged 6, was subjected to a combination therapy with plasmochin and atabrine. This boy developed a laryngeal spasm with partial paralysis of the respiratory muscles. In both cases the respiratory disturbances became intensified during sleep. In the second case a decided improvement of the respiratory disturbances could be obtained by injections of thiamin chloride.

Oto-Rino-Laringologia Italiana, Bologna

10: 1-86 (Jan.) 1940. Partial Index

Clinical Behavior and Semeiotics of Respiratory Tract in Laryngectomized Persons. C. Baccarani.—p. 43.
*Therapy of Pain After Tonsillectomy by Vitamins B_1 and C. M. Baer.—p. 65.

Vitamins in Treatment of Pain from Tonsillectomy.—Baer observed a considerable number of cases of tonsillitis, during the past year, in which tonsillectomy was performed under local anesthesia. He states that inflammation of the tonsils is frequently associated with vitamin B_1 and C hypovitaminosis and with actual or latent rheumatism. He believes that local pain during the first twenty-four hours after tonsillectomy is due to the wound itself and to exposure of the nerve ends in the wound, whereas that which is present on the second day is due to B_1 and C hypovitaminosis, either alone or in association with rheumatism. The treatment of early local pain consists of administration of analgesics. The author was able to demonstrate a prompt favorable action with vitamins B_1 and C in fifty patients in his group who were suffering from local pain late in the postoperative period. He used two preparations, precise doses of which are not specified. In all cases the treatment caused rapid regression of local pain, improvement of the general condition and acceleration of the local process of healing.

Revista de la Asoc. Méd. Argentina, Buenos Aires

53: 1171-1238 (Dec. 30) 1939. Partial Index

*Encephalitis in Whooping Cough. F. Bazán and R. Maggi.—p. 1171.
Friedman's Reaction in Testicular Tumors. J. M. Lascano Gonzalez and R. I. Mathis.—p. 1205.

Encephalitis in Course of Whooping Cough.—Bazán and Maggi report their observations made from 1936 to 1939 in the department of infectious diseases in a pediatric hospital in Buenos Aires. Of 600 children with whooping cough, fifteen (eleven infants and four children ranging in age from 3 to 6 years) developed acute encephalitis, as a rule in the third week. They found that the course of encephalitis complicating whooping cough varies with the age of the patient, the clinical form and type of encephalitis and whether there were bronchopneumonic complications or otitis. The younger the patient the more grave the nervous complications. These may be acute, subacute or chronic with a predominance of convulsions, somnolence, paralysis, polyneuritis, ataxia, choreo-athetosis, poliomyelitis, and sensory and psychic disturbances. Convulsive forms are the most frequent. The cerebrospinal fluid either is normal or shows a moderate lymphocytic reaction. The prognosis is grave (a mortality rate of 80 per cent in grave forms of encephalitis and the development of psychic, motor or associated psychomotor sequels in 50 per cent of subacute cases). The condition is due to a toxic infection the nature and mechanism of which

are not clear. The treatment consists of administration of drugs to control convulsions, the general toxic infection and associated infections, baths, antispasmodic drugs, anesthetics, lumbar puncture for the convulsions, methenamine, a combination of cinchophen and methenamine, intravenous administration of hypertonic dextrose solution, colloidal metals, protein therapy, abscess of fixation and sulfanilamide. Associated infections are treated and vaccines against whooping cough are administered according to indications. It is advisable to watch and stimulate the functions of the cardiovascular system and to improve the organic resistance of the patients. If sequels remain, massage, electrotherapy, gymnastics and psychic reeducation are indicated. In the group of cases reported by the authors there were twelve deaths (all, but one, of infants). Necropsies performed in nine demonstrated that the pathologic lesions are not typical for whooping cough. They consist of degeneration, inflammation and hemorrhages.

Semana Médica, Buenos Aires

47: 365-424 (Feb. 15) 1940. Partial Index

*Administration of Ascorbic Acid to Infants. J. R. Mendilaharzu and E. L. Zavala Rodriguez.—p. 365.
Cesarean Section Due to Sclerosis of Neck of Uterus from Diathermocoagulation. J. L. Ahumada.—p. 377.

Administration of Ascorbic Acid to Infants.—Mendilaharzu and Zavala Rodriguez observed a large group of infants at the institution of puericulture in Buenos Aires. They were suffering from purpura haemorrhagica, stomatitis and glossitis, dystrophy or infections (whooping cough, pneumonia and congenital syphilis). The treatment consisted of daily intravenous injections of 0.1 Gm. of ascorbic acid up to a total dose of 1 Gm. in ten days, or of intramuscular injections of from 0.2 to 0.5 Gm. up to a total dose of 2.5 Gm. in seven days. The authors found it advisable to administer liberal amounts of ascorbic acid to infants who are artificially fed, as well as in the course of fevers and gastrointestinal disease (during which the organic needs for vitamin C are greater than they are in normal conditions). Satisfactory results were obtained from the treatment as specified in one case of purpura haemorrhagica and in eleven of thirteen cases in which there was acute stomatitis and glossitis. It also proved satisfactory in dystrophy when administered in association with other vitamins. The treatment had no effect in whooping cough and pneumonia or in congenital syphilis when administered along with arsphenamine. It had no effect on the tolerance of the patient for arsphenamine.

Archiv für Dermatologie und Syphilis, Berlin

179: 463-572 (Nov. 23) 1940. Partial Index

Experience with Acetylsulfanilamide in Treatment of Gonorrhea. Dahlenburg.—p. 463.
*Etiology and Therapy of Mycosis Fungoides. M. Niethammer.—p. 484.
Does Use of Acetylsulfanilamide or Dimethyl Disulfanilamide Produce Impairment of Liver? Remarks on General Cutaneous Eruptions. F. Schaefer.—p. 500.
Liver and Spleen Extracts of Rabbits Immunized Against Syphilis in Treatment of Late Syphilis, with Special Consideration of Hepatic Syphilis. G. Kertész.—p. 510.
Deep Blastomycosis of Skin: Case. R. Richter.—p. 517.
Noma-like Clinical Picture Produced by Blastodendrion Palati. W. Fröhlich, F. Zach and W. Piringer.—p. 521.
*Microscopy with Aid of Fluorescence Under Mercury Lamp Illumination and Capillaroscopy in Dermatologic Studies. Schmidt-La Baume and R. Jäger.—p. 531.

Etiology and Therapy of Mycosis Fungoides.—Niethammer enumerates several theories regarding the pathogenesis of mycosis fungoides and states that the majority of investigators regard it as an infectious process. He reviews the literature, which supports the infectious etiology, and presents a case in which the cutaneous lesions yielded a strain of streptococci, partly in pure culture; the strain was characterized by the formation of atypical forms. The same strain of streptococcus could be cultured from two cases of mycosis fungoides at the university clinic in Cologne. The antigens produced with these strains gave positive complement fixation with two serums from mycosis fungoides. However, the strains failed to show demonstrable pathogenicity for either rabbits or guinea pigs, so that nothing definite could be said about their etiologic significance in this disease. The author points out that favorable therapeutic results have been obtained in mycosis fungoides with mono methyl-disulfanilamide and with disulfanilamide.

Fluorescence Microscopy and Capillaroscopy in Dermatology.—Schmidt-La Baume and Jäger state that heretofore dermatologists have been able to study the surface structure of the skin to only a limited extent because of the lack of an efficient microscopic method. They demonstrate that pure surface pictures of the living skin not distorted by pictures of the deeper layers can now be obtained with a microscopic method developed by R. Jäger and F. Jäger. In this method the skin is stained with a fluorescent dye that is invisible in daylight but assumes a yellowish green fluorescence under irradiation with long wave ultraviolet and visible violet rays. A 1 to 5 per cent aqueous solution of primulin is rubbed on the area of the skin that is to be examined. The area is placed under an ultramicroscope and the fluorescence of the dye is stimulated by means of a mercury vapor lamp. The light of the lamp is passed through a special filter which passes only the ultraviolet, violet and blue parts of the light. In order to avoid interference by the stimulating lamp, another filter is placed between the objective and the ocular; this filter passes only light that has a wavelength exceeding that of the stimulating lamp. Thus only the true fluorescent light reaches the eye of the observer or the photographic plate. In this way the method produces pure surface pictures. The authors stress the advantages of the mercury vapor lamp over the large arc lamps formerly used for fluorescence microscopy. The same instrumentarium can be used for depth pictures. Good pictures of the capillaries can be obtained by omitting the filters and working with white light. Thus it is possible to observe successively a surface picture and a capillary picture of the same area of the skin. The authors reproduce a number of photomicrographs of the normal skin, of different skin lesions, of the course of the capillary reaction in case of a positive cutaneous test and of the changes in emulsions that are applied to the skin. The authors are convinced that the method will prove of great value not only in dermatology but also in industrial hygiene.

Archiv. f. exper. Pathologie u. Pharmakologie, Berlin

193: 505-735 (Nov. 24) 1939. Partial Index

Determination of Action Value of Estrus-Producing Hormone Tablets Available on the Market. W. Koll and F. Kölz.—p. 505.
*Experimental Investigations on Elimination of Thallium in Various Body Fluids. J. Frey and Maria Schlechter.—p. 530.
Studies on Formation of Methemoglobin. B. von Issekutz Jr.—p. 551.
Inhibitory Effects of Oxidized Epinephrine. E. Sanders.—p. 572.
Thyroxine and Heart Action. H. Bauer.—p. 642.
Relations Between Anterior Lobe of Hypophysis, Thyroid and Adrenals in D Avitaminosis. E. Schulze and M. Flach.—p. 727.

Elimination of Thallium.—Frey and Schlechter report experimental investigations on the elimination of thallium in various body fluids. Their studies were prompted by a case of criminal thallium poisoning. The vomit of the woman in question contained moderate quantities of thallium as late as the thirty-fifth day after onset of the poisoning, whereas the feces contained a smaller amount of poison. The authors studied thallium poisoning in rabbits. Poisoning was produced by the subcutaneous injection of an aqueous solution of thallium acetate. The spectrographic procedure of Gerlach served for the quantitative determination of thallium in the peripheral blood, blood of the portal vein, gastric juice, cystic bile, small and large intestine, feces, urine, milk, placenta and the fetal tissues. It was found that thallium is eliminated chiefly by way of the kidneys. Thallium appears in the gastric juice a few minutes after the injection of the toxin. The concentration here depends on that of the blood but never becomes quite equal to it. In following the thallium content in the intestine, it was found that in the upper portion of the small intestine it is extremely high, for here it exceeds the concentration in the blood. Toward the middle portion of the colon it decreases somewhat and in the terminal portion of the intestine the thallium concentration again reaches that of the blood. The authors think that the increase of the thallium concentration in the upper portion of the small intestine is due to the addition of the cystic bile with its high thallium content; the decrease in concentration in the terminal portion of the intestine is accomplished by the inspissation of the colonic contents. Regarding the retroresorption of the thallium from the intestine, the authors assume that this portion of thallium returns to the liver with the blood of the portal vein, for they observed that the thallium concentration of the blood

of the portal vein was higher than that of the peripheral blood; thus thallium is influenced also by the enterohepatic circulation. Thallium enters the milk in a concentration that is slightly below that of the blood. The placenta was found to be permeable for thallium. The fetal heart, brain, liver and kidney contained the poison in considerable quantities. Pregnant animals have a higher resistance to the poison than nonpregnant animals. The abortifacient effect of thallium was corroborated. These observations on the elimination of thallium are of therapeutic significance. They suggest that efforts should be made to increase the diuresis, since the kidney is the chief organ of elimination for thallium. Because of the enterohepatic circulation of thallium, the authors recommend the use of saline cathartics. Gastric lavage with simultaneous stimulation of the gastric secretion by histamine may be of aid in the removal of thallium.

Beiträge zur Klinik der Tuberkulose, Berlin

94: 1-98 (Nov. 21) 1939. Partial Index

Work Insufficiency Due to Respiratory, Cardiac and Nervous Diseases. H. W. Knipping and G. Matthiessen.—p. 1.
Mechanism of Healing of Tuberculous Cavities: Pathologic-Anatomic Study. J. Mille.—p. 26.
*Tuberculosis Fungosa Serpiginosa, A Senile Form of Cutaneous Tuberculosis. H. Hamann.—p. 64.
A Ten Year Retrospect in the Cultivation of Koch's Bacillus. C. Coronini.—p. 91.

Serpiginous Tuberculosis of Skin.—Hamann reports two cases of tuberculosis fungosa serpiginosa cured by scraping with a sharp spoon and application of pyrogallol. The first patient, aged 72, had a swelling first on the left forearm. It gradually increased. Two years later an ulcerous spot appeared on the left hand and extended to the forearm. The roentgenogram disclosed bone tuberculosis of the left ulna. Tubercle bacilli were readily found in the papillomatous infiltrations. The second patient, aged 61, had a small brown spot on the back of the right hand, which rapidly enlarged. Examination of the lungs showed tuberculosis in the right upper lobe. Tubercle bacilli were readily demonstrated in the papillomatous formations. According to the author, the disease is confined almost entirely to persons past the age of 60 and its course is relatively benign. It is usually localized on the back of the hand and on the forearm. The clinical picture is one of a cutaneous tuberculosis that rapidly extends in all directions and forms a central scar. It exhibits three zones, the central zone predominating. In the vicinity of the cicatrization, yellow-brownish spotted infiltrations develop with colloidal degeneration of the connective tissue. The peripheral outer zone presents a muddy blue-red infiltration and a tightly drawn skin, the middle zone an ulceration with papillomatous proliferations. These proliferations form clusters between which are found ulcerating surfaces covered with pus. Minute tubercles are abundantly found in the infiltrations. A pronounced necrosis is seldom observed. In the majority of the cases the disease arises from a subcutaneous tissue tuberculosis, but it may also be caused by an external superinfection. The author discusses the differential diagnosis of similar conditions. The disease is comparatively rare. Only seven cases were observed within eighteen years in the university clinic in which this study originated.

Deutsche Zeitschrift für Chirurgie, Berlin

252: 677-764 (Nov. 24) 1939

Development of Cancer on Chronic Inflammatory Basis. W. Pohl.—p. 677.
Pathology and Therapy of Atraumatic False Aneurysms. W. E. Künstler and V. Ghiron.—p. 693.
Case of Lung Fluke Disease of Brain (Paragonimiasis s. Distomiasis Cerebri); Successful Operation. N. Kawai.—p. 705.
*Foundations for Surgical Treatment of Esophageal Varices. D. M. Juzbašić.—p. 711.
Pathologic and Clinical Aspects of Nonparasitic Splenic Cysts. V. Pika and H. Šikl.—p. 746.

Treatment of Esophageal Varices.—Juzbašić presents a detailed study of the present status of the problem of the esophageal varices. He emphasizes that various developmental types and stages of extension necessitate different operations. He pays particular attention to the esophageal varices which develop on the basis of portal hypertension. He is of the opinion that every procedure which has the radical removal of esophageal varices as its aim must fulfil two requirements: 1. Measures must be taken to prevent the portal vein from sending its blood into the vena cava by way of the esophagus. 2. A new but less dangerous blood passage must take the place of the interrupted one. In order to determine exactly what afflux passages must be interrupted and at what sites, the author made a number of experiments on cadavers with esophageal varices. He first introduced a dyestuff into the vena mesenterica superior and then executed the necessary interruptions. He then tested the correctness and efficacy of the interruptions by subsequent injection of another dyestuff, again into the vena mesenterica superior. On the basis of these experiments he suggests a surgical method which comprises three stages: (1) interruption of all venous afflux passages that pass through the lesser omentum, (2) interruption of the venous afflux passages from the splenic region and (3) production of a new discharge passage for the blood of the portal vein into the vena cava by means of one of the modifications of Talma's operation.

Monatsschrift für Kinderheilkunde, Berlin

81: 1-138 (Dec. 11) 1939. Partial Index

Serum Therapy in Pneumonia of Children. Erika Hering.—p. 1.
Dysostosis Enchondralis. K. Schwartzer and W. Middelkampf.—p. 17.
Fetal Polyglobulism. E. Loeschcke and K. Schwartzer.—p. 25.
*Allergic Tests in Asthma and Other Allergic Diseases of Children. Gertrud Becker.—p. 63.
Nonspecific Therapy in Epidemic Meningitis. Ingrid von Rieben.—p. 102.

Allergic Tests in Bronchial Asthma of Children.—Becker reports the results of allergic tests performed during the course of five years in a university clinic on eighty-seven children presenting bronchial asthma or bronchial spasms. The age level of the children (sixty-four boys, twenty-three girls) was between 2 months and 16 years, the majority between 3 and 10 years. More than a third of the children were rural. The testing materials consisted of different proprietary allergy extracts combined, for purposes of time saving and economy, into compatible aggregates that yielded six test divisions: (1) bacterial allergens; (2) animal scale allergens; (3) domiciliary allergens containing human skin scales, mold-fungi, bedfeathers, house dust and grain mites; (4) food allergens; (5) pollen antigens, and (6) multiple susceptibility. Combined tests were followed up by single tests after the group was determined. The intracutaneous method was employed as the method of choice. Positive reactions were obtained in sixty-eight of the eighty-seven children (78 per cent) and were separated into a series of tables. The largest incidence was discovered in group 1 with fourteen, group 2 with sixteen and group 6 with thirty-one. Children presenting bronchial asthma frequently (one third of the total) had been affected with eczema in early childhood or with gastric disorders. Twenty-five per cent of the children were susceptible to seasonal change or foggy weather. An increase of eosinophil cells was noted during asthmatic attacks. Typical asthma was rare. The Moro reaction applied to forty-nine children was positive in eleven cases. The author recommends the use of allergic tests in children for prompt early diagnosis of a probable allergic etiology and its prompt treatment.

Röntgenpraxis, Leipzig

11: 651-728 (Dec.) 1939. Partial Index

Hyperostosis of Frontal Bone. L. Richter.—p. 651.
*Aspects of Patella Cubiti (Elbow Cap). G. Theising.—p. 663.
Pneumonic Round Shadows. H. Oeser.—p. 676.
Lateral X-Ray Exposure in Diagnosis of Renal Calculi. D. Knuth.—p. 679.
Simulation of Pulmonary Process by Hair Braid in Roentgenologic Examination. W. M. H. Weisswange.—p. 690.

Patella Cubiti (Elbow Cap).—Theising discusses the anomalies of the extensor side of the elbow joint, the so-called "patella cubiti," the "elbow cap" or the "os epiphyseos olecrani." He reviews twenty-two cases from the literature and describes two cases of his own in which trauma was responsible for an avulsion fracture of the olecranon. Formation of new bone by the detached periosteum and intratendinous calcification as the result of hemorrhage led to the formation of a compact osseous body above the olecranon. He cites the views of other investigators regarding the various types of anomalies on the extensor surface of the elbow joint and presents his own classification. He differentiates patella cubiti of the first, second and third degree. The first degree of patella cubiti is represented by the persistent cartilaginous epiphysis between the ulnar portion of

the olecranon and the apophysis. This form is not movable. The second degree is represented by the completely developed anomaly, which is isolated, is movable, articulates and is located above the almost normal olecranon. This type he designates as patella cubiti or os epiphyseos olecrani. An olecranon that is completely isolated from the ulna is identified as the patella cubiti of the third degree. In this case the proximal end of the ulna is almost circular and is connected with an olecranon which has become a true patella cubiti by strands of connective and tendinous tissues. This anomaly may easily be confused with the pseudarthrosis that develops following a typical olecranon fracture. Avulsions of periosteum and bone, as well as their proliferations, represent the fourth group of anomalies in the elbow joint, intratendinous and intramuscular ossifications resulting from chronic or acute traumas the fifth group and true sesame bones (in Pfitzer's definition) the sixth group.

Zeitschrift für Kinderheilkunde, Berlin

61: 423-532 (Dec. 22) 1939. Partial Index

Polycythemia Vera: Case. O. Göbell.—p. 423.
"Yellow Stools." W. Brenner and W. von Harpe.—p. 434.
*Prognosis in Spastic Bronchitis of Infants. B. Köhler and H. Mai.—p. 481.
Vitamin D Formation in Skin. H. Mai.—p. 503.
Effect of Short Waves on Diphtheria Bacillus. E. Hasché.—p. 506.

Spastic Bronchitis of Infants.—Observations based on a ten year study in a university clinic of 111 cases of children presenting spastic bronchitis, with and without familial anamnesis, indicate to Köhler and Mai corroborative evidence for the possibility of the evolution of infant spastic bronchitis into subsequent bronchial asthma. Of the 111 children, twenty-five were eliminated from further study because a definite familial connection could not be determined. The familial investigations included kindred exudative manifestations such as urticaria, eczema and arthritis. Sixty-two per cent of the children (contrasted with a 22.5 per cent of a numerically equal control group) showed familial implications with the following distribution: seventeen (19.5 per cent) bronchial asthma, twenty-eight (33 per cent) eczema, gout, rheumatism, migraine and so on, eight (9.5 per cent) "chronic coughing," and others of which the exact alliance was not determinable. Thirty-eight per cent of the children possessed no familial history of the disease. On further investigations the authors found that poor reactions to ephetonine in cases of spastic bronchitis without familial involvements did not constitute proof that such spastic cases were simple cases of bronchitis and never evolved into bronchial asthma. Of twenty-six children observed without a familial disease background eighteen reacted poorly to ephetonine but showed latent asthma. On the other hand, eighteen of twenty-seven children with a familial history who had contracted spastic bronchitis during their first year of life were long afflicted with spastic attacks or stubborn bronchitis (observation time from four to five years). Furthermore, in twelve children belonging about equally to these two groups a clear evolution of spastic bronchitis into true asthma was noted. The authors accept the view that infant asthmas represent nervous involvements of an exudative diathesis and that a close connection exists between infant bronchitis and related exudative diseases.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

84: 281-380 (Jan. 27) 1940. Partial Index

*Application of Convulsion Therapy by Means of Electric Shock. J. A. J. Barnhoorn.—p. 290.
Kojewnikoff's Syndrome: Continuous Epilepsy. J. J. H. M. Klessens.—p. 301.
Elimination of Large Gallstone Through Surgical Wound in Region of Appendix. B. J. de Haan.—p. 305.
Vagotinine (Pancreatic Hormone). K. van Dongen.—p. 307.

Convulsion Therapy by Means of Electric Shock.—Barnhoorn directs attention to the electric shock therapy developed by Cerletti and Bini (abstracted in THE JOURNAL, Dec. 2, 1939, p. 2100). He describes the apparatus and reports his experiences in thirty-five cases in which 266 attacks were provoked. He compares the technical value of this method with that of the metrazol shock therapy of Meduna. The therapeutic value of the method cannot be estimated as yet, but the author thinks that the electric shock therapy signifies considerable progress in the application of convulsion therapy in psychoses. The method has a number of advantages: It is easily applied and it produces immediate loss of consciousness and complete amnesia. This is important because it eliminates the anxiety, and the patient's objection to the treatment is overcome. Moreover, the patient rapidly recovers and there are no unpleasant after-effects and secondary reactions. The method seems to be harmless.

Acta Chirurgica Scandinavica, Stockholm

83: 385-477 (Jan. 27) 1940

Occurrence of Double Processus Vermiformis. J. Adams-Ray.—p. 385.
*Postoperative Thrombosis: Preliminary Study. G. Bergquist.—p. 415.
Four Cases of Chordotomy with Microscopic Examination of One Case. E. Platou.—p. 435.
Treatment of Fracture of Corpus Mandibulae ad Modum Ipsen. P. Søbye.—p. 445.

Postoperative Thrombosis.—According to Bergquist, prophylaxis against postoperative thromboses can be promoted by a daily analysis of the blood coagulation time before and after the operation and by the regular determination of the thrombocytic count. Employing Kristenson's pipet for the latter and Petrén's procedure for the former (normal coagulation level from three to five minutes) and administering heparin when needed, the author was able to avoid thrombotic or embolic complications in fifty cases so controlled. In eight of these cases heparin was deemed necessary. He verified the observation that, whereas thrombocytes did not increase appreciably, the blood coagulation time had a tendency to fall below the lowest normal level (three minutes) between the fifth and the eighth day and occasionally as late as the tenth. Whenever this tendency occurred he administered intravenously 0.6 cc. of a 5 per cent solution of heparin. He retested after four hours. If a subnormal tendency continued, he injected an additional 1 cc. A retest was made after six hours and 2 cc. administered, if necessary. The test was repeated seven or eight hours later. To avoid loss of time and vein lesions due to frequency of venous punctures for blood sampling and intravenous application of heparin, the author tested the blood coagulation time in twenty persons (equally divided between the sexes) both by venous and by digital extraction. In general, no difference appeared in the blood levels. On the other hand, the subcutaneous administration of heparin was found to produce more painful hematomas. The author holds the generally accepted view of the etiology of thrombosis (modification in the blood stream, biochemical changes in the composition of the blood, possible endothelial lesions) but believes that vortex formations in the circulation in postoperative cases cause a prethrombotic condition, which however can be controlled and guarded against by daily blood coagulation tests. He does not believe that the coagulation time needs to be elevated to three or four times the normal level in order to insure prophylaxis but has come to think that a one minute drop may constitute in individual cases an idiopathic danger signal of a prethrombotic condition even if the minimum three minute level has not been reached.

Ugeskrift for Læger, Copenhagen

102: 27-56 (Jan. 11) 1940

*Alkali Treatment in Diabetic Coma with Hyperazotemia and Anuria. N. B. Krarup.—p. 27.
Extent of Lupus Vulgaris in Denmark. C. N. S. Gundtoft.—p. 32.
Simplification of Technic in Diagnosis of Tissue. V. Eskelund.—p. 38.
Bilateral Leiomyoma of Epididymis. J. Fogel.—p. 39.

Alkali Treatment in Diabetic Coma with Hyperazotemia and Anuria.—Krarup reports a typical case of the so-called renal form of diabetic coma. On the third day the blood sugar was well regulated, the ketonuria had disappeared, the plasma chloride was normal and there were no signs of failing circulation, but the alkali reserve was still low. The blood urea increased and anuria developed, with aggravation of the general condition. After isotonic sodium bicarbonate intravenously (1 liter of a 1.3 per cent solution daily for three days) the alkali reserve rose, the flow of urine was reestablished and there was ultimate complete restoration of renal function. The origin of the syndrome in the renal form of diabetic coma is ascribed to the acidosis, or deficiency of fixed alkali. Isotonic sodium bicarbonate intravenously after determinations of the alkali reserve is considered the most rational therapy.